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ESOPHAGEAL ATRESIA WITH TRACHEOESOPHAGEAL FISTULA*

Epidemiologic and Teratologic Implications

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THE causative agents of atresia of the esophagus must be primarily genetic or else act during prenatal life, for the defect is present at birth. The evidence bearing on the subject has been brought together here for analysis, and is presented as a stimulus to further research on the problem of etiology.

This report is based on a study of 107 infants with esophageal atresia (102 with associated tracheoesophageal fistula) seen at the Children's Hospital from January, 1936, through 1948 or born at the Boston Lying-in Hospital (6 cases) between 1934 and 1945, inclusive; 90 died during infancy and the autopsy records of 70 were available for study. Also included are 10 histories of pregnancy terminating in the birth of a child with the anomaly. The clinical data were noted in case records of the Children's Medical Center in Boston, or gained by correspondence with attending physicians.

CLINICAL DESCRIPTION

One of the first case reports ever published still remains an illuminating and compact description of the basic symptomatology and pathology. Thomas Gibson[1] described this case as follows:

> About November, 1696, I was sent for to see an infant that could not swallow. The child seemed very desirous of food and took what was offered it in a spoon with greediness, but when it went to swallow it, it was like to be choaked; and what should have gone down, returned by the mouth and nose, and it fell into a struggling convulsive sort of a fit upon it. It was very fleshy and large and was two days old when I was called to it but the next day died.
>
> The parents being willing to have it opened, I took two physicians and a surgeon with me. . . . We cut open the thorax and taking out the gullet (with the windpipe, lung, etc.,) continued to the stomach. Then we made a slit in the stomach and put a pipe in its upper orifice, and blowing, we found the wind had a vent, but not by the top of the gullet. Then we carefully slit up the back side of the gullet from the stomach upwards, and when we had gone a little above half way toward the pharynx we found it hollow no further. Then we began to slit it open from the pharynx downwards, and it was hollow til within an inch of the other slit, and in the imperforate part it was narrower than in the hollowed. This isthmus (as it were) did not seem ever to have been hollow, for in the bottom of the upper and the top of the lower cavity there was not the least print of any such thing, but the parts were here as smooth as the bottom of an acorn cup.
>
> Then searching which way the wind had passed when we blew from the stomach upwards, we found an oval hole (half an inch long) on the fore side of the gullet opening into the aspera arteria, a little above its first division, just below the lower part of the isthmus above mentioned.

This is a perfect description of the commonest type of esophageal atresia, the lower trachea (aspera arteria) communicating with the distal esophagus, the proximal portion being atretic.

EPIDEMIOLOGY

Many points of epidemiologic importance were not covered in each of the 107 records reviewed. Therefore in some of the following sections the series total is expressed as less than 107 by reason of excluded records — those not contributing to the specific data sought. To determine the frequency with which esophageal atresia occurs, the obstetric experience at the Boston Lying-in Hospital was studied. In addition the epidemiologic observations of previous investigators[2-4] are combined here for analysis.

Because esophageal atresia is frequently accompanied by tracheoesophageal fistula (84 per cent of 245 cases[4]) the two conditions have nearly always been studied as one entity. For purposes of brevity the term tracheoesophageal fistula is hereafter abbreviated as TEF, and broadly used.

Frequency

Six cases of TEF (1 in a stillborn infant) among 30,497 live births were found in the records of the Boston Lying-in Hospital for the years 1934 to 1945, inclusive. On this basis the frequency of TEF, in the Boston area, may be estimated as at least 0.2 per 1000 live births, the major variable prob-

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ably being the missed case — the stillbirth and asphyxial death in which no autopsy was performed.

All observers are agreed that esophageal atresia is a rare condition. Murphy[5] found 13 cases recorded on death certificates in Philadelphia during a five-year period when 166,451 live births occurred — not quite 1 per 10,000 live births.

Case Mortality

Before surgical methods were applied to the treatment of TEF, survival was a rare accident dependent on the existence of a defect so small as to be of no critical consequence. Plass[2] assembled data relative to the length of life of 120 babies with the anomaly as shown graphically in Figure 1. Five were still-

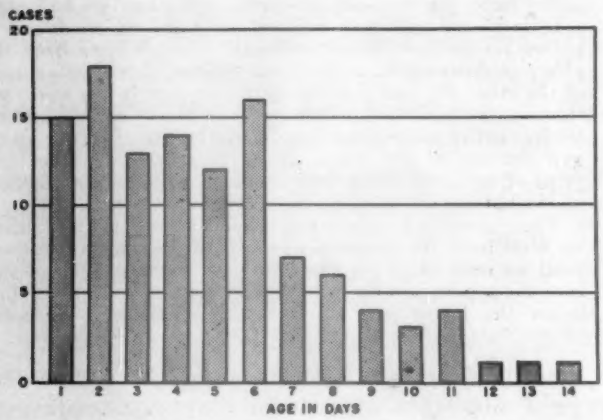

FIGURE 1. *Age at Death of 115 Babies with Tracheoesophageal Fistula (Based on Data of Plass[2]).*

born. Mean survival time for the other 115 may be calculated as 4.8 (± 3.5) days.

Swenson[6] reports that with modern surgery 57 of 113 patients operated upon in the last eight years at the Children's Hospital, Boston, have survived, and only 5 postoperative deaths have occurred in the last 32 patients.

Familial Occurrence

None of the families of the 107 infants in this series was known to include another member with esophageal atresia or TEF either in the same or in a preceding generation.

Among the histories of 136 babies with esophageal atresia Plass[2] found none with multiple familial occurrences, but Lanman,[7] in 1940, reported the condition in a brother and sister, born one year apart. No case of the anomaly recurring as a familial trait in successive generations has been encountered in a comprehensive review of the literature on the subject.

Sex Incidence

There were 62 male infants and 45 females in this series. Added to 25 males and 19 females in two previously reported series,[2, 4] a ratio of 87 (57.6 per cent) males to 64 females is obtained. Normal expectancy for Massachusetts, 1939 to 1943, inclusive,[8] is 52.6 per cent males; the difference is not significant.

Birth Weights

Birth weights recorded for 87 infants with TEF were significantly lower than those of 1000 babies of a general lying-in-hospital population, as shown in Figure 2. The birth weight of 18 of these infants whose mothers had hydramnios averaged 5 pounds, 2 ounces, that of the remaining 69 averaging 6 pounds, 1 ounce.

Relation to Maternal Factors

Age. The ages of 75 mothers who gave birth to a baby with TEF are compared with those of mothers in Massachusetts during the years 1939 to 1943, inclusive (Table 1). The disease appeared more frequently than was to be expected by chance among the progeny of older women, though this trend is far less striking than that for mongolism.[9]

Maternal marital status. Four of 102 mothers (39.2:1000) were unmarried (a fifth, though married, had the baby illegitimately), normal expectancy for the general white population United States Registration Area, 1939 to 1944, inclusive,[8] being 18.4/1000.

Previous miscarriages and stillbirths. The birth of 19 of 79 infants with TEF had been preceded by a miscarriage or stillbirth, 12 by one, 4 by two, and 3 by six such pregnancies. The 79 mothers had a total of 277 conceptions, of which 32 (11.6 per cent) ended in spontaneous abortion, as compared with an incidence of 10.6 per cent in 1150 pregnancies over a six-year period studied by Hertig and Livingstone[10] in a private practice at the Boston Lying-in Hospital.

Birth order of the affected child. In 76 records 30.3 per cent of the mothers were found to be primiparas. According to Gates[11] 41.2 per cent of children in Canada are expectedly first-born. Expectancy for this series computed by the Greenwood–Yule rule[12] is given in Table 2. As in mongolism[13] the risk was found to be greater with each successive pregnancy.

Maternal health. Among 87 case records evidence of chronic maternal disease during pregnancy was encountered 12 times. Hyperemesis gravidarum was noted 3 times; 3 mothers had goiter; 3 had pre-eclampsia, and 3 others had pelvic deformities; 2 had chronic pyelitis; and 1 had tuberculosis with effusion and pneumothorax. The significance of such findings is problematic. Acute illnesses and ante-partum hemorrhages that could be localized in time tended to occur in early pregnancy as shown in Table 3 and 4.

Unusual placental environment. The clinical observation of earlier writers[2, 14] that a significant

association exists between TEF and maternal hydramnios was confirmed by finding of the condition 20 times among 87 mothers. In addition, abnormalities of the placenta (Table 4) were encountered frequently enough to suggest that particular search for similar associations should be made in the future. Four pairs of twins as the product of 107 births is four times expectancy, although the finding could be due to chance.

The following brief case reports suggest a relation of TEF to maternal or placental factors.

Case 1. A 30-year-old woman with a goiter of about 15 years' duration had had nine pregnancies resulting in living children of whom only the seventh is known to have had a congenital anomaly (of the heart). During the tenth pregnancy the mother developed hydramnios, and at term the baby was found to have TEF. A subsequent pregnancy resulted in a living child, a twelfth in a miscarriage in the 6th month, and a thirteenth in a living child.

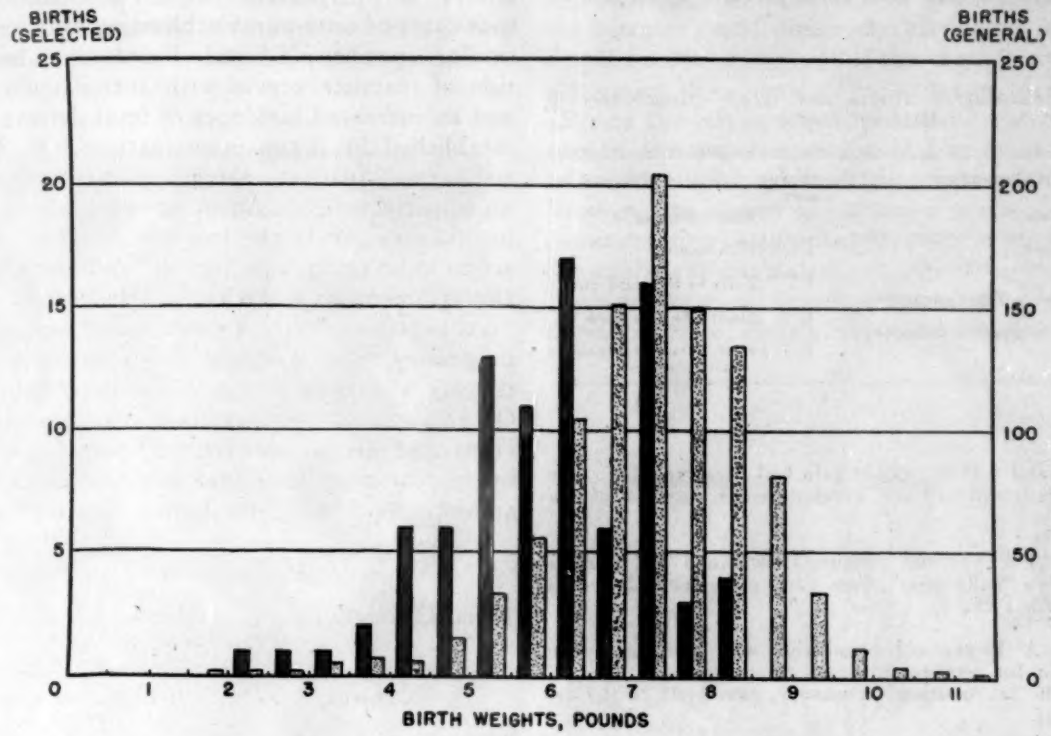

Figure 2. *Distribution of Birth Weights of 1000 Living Babies of a General (Lying-In) Hospital Population (Stippled Bars) and 87 Living Babies with Tracheoesophageal Fistula (Shaded Bars).*

Table 1. *Maternal Age and Esophageal Atresia.**

Maternal Age	Births	
	Infants with Esophageal Atresia	General Population Massachusetts (1939–1943)
yr.		
15–19	5	18,911
20–24	16	99,185
25–29	20	114,040
30–34	19	78,094
35–39	14	37,611
40–44	0	9,909
45–49	1	650

*Among 75 mothers of infants with TEF, the mean age was 29.17 yr. (standard deviation, 6.285). Among 358,400 mothers in the general population the mean age was 28.18 yr. (standard deviation, 5.880). The difference of the means was 0.99, and the standard deviation of the difference, 0.229. The critical ratio was 4.3.

Case 2. A 20-year-old primipara gave birth to twins after a pregnancy complicated by hydramnios. Excess fluid was observed in the amniotic sac of 1 infant with TEF (who also exhibited mongoloid features) but not in that of its normal fellow.

Case 3. A 31-year-old woman had had a miscarriage, and irregular periods prior to conception of the baby with TEF. Pregnancy was characterized by frequent bouts of sore throat with low-grade fever. During the 4th and 5th weeks while traveling by rail during the summer of 1943 she was without drinking water for over 24 hours and developed "heat prostration," with a temperature of 104 to 105°F. for 2 days. A third pregnancy, again associated with intermittent

Table 2. *Birth Order among 76 Infants with Tracheoesophageal Fistula.*

Birth Order No.	Observed	Expected %	Expectancy %
1	23	41.75	55
2	26	18.75	139
3	9	5.75	152
4	3	2.75	109
5	4	2.08	192
6	2	1.28	156
7	2	0.95	215
8	2	0.66	303
9	2	0.41	488
10	1	0.19	527
11	1	0.09	1,111
18	1	—	—
Total	76		

sore throats, ended in the birth of a normal infant. Chronically infected tonsils were subsequently removed with relief of symptoms referable to the throat.

CASE 4. A 38-year-old previously married woman had had two pregnancies resulting in a normal child, and a miscarriage (at 6 weeks) 2 years prior to the birth of a baby with TEF. Hydramnios had been noted as early as the 6th or 7th month, and a 35-lb. weight gain had been recorded. The placenta was found to have a velamentous insertion of the cord.

TABLE 3. *Esophageal Atresia and Acute Disturbances of Maternal Health.*

ACUTE DISTURBANCE	OBSERVED CASES	STAGE OF GESTATION
Pneumonia (Case 7)	1	First trimester
Appendectomy with uterine suspension (Case 6)	1	First month
Attempted abortion — quinine (Case 10)	1	Early in the third month
Sore throat with heat prostration (Case 3)	1	Fourth to fifth week
Acute upper respiratory infections (Case 9)	1	First trimester; again in last trimester.

CASE 5. A 19-year-old primipara, who had had pyelitis treated with a "sulfa drug" from early pregnancy, delivered an infant with TEF.

CASE 6. A 19-year-old primipara, who had undergone an operation for appendicitis and correction of a "tipped womb" in the 1st month of pregnancy, gave birth to the defective infant.

CASE 7. A 24-year-old mother, whose one previous pregnancy had ended normally, developed pneumonia at the end of the 1st month of her next pregnancy. The infection lasted about 4 weeks and was treated with one of the sulfonamides. At term the baby was found to have TEF.

CASE 8. A 48-year-old woman had had 11 living children and 6 miscarriages. She had been operated upon for a ruptured appendix and for goiter during the 3 years preceding the 18th pregnancy, which was complicated by symptoms of pre-eclampsia and resulted in a defective infant.

CASE 9. The third pregnancy of a 35-year-old woman whose previous 2 children were normal resulted in a baby with TEF. She had suffered from a severe cold and cough during the first and "grippe" during the last trimester of gestation. Subsequently a fourth, normal child was born.

CASE 10.* The mother stated that she had taken 30 pills of quinine sulfate (30 gm.) early in the 3rd month of her pregnancy to induce abortion.

The same data that suggest a relation between TEF and an unusual placental environment raise the possibility that the fetal disease is secondary to disturbances of the maternal organism or placenta. As long ago as 1867 Dareste[15] described thermal injuries of the developing hen's egg, which resulted in arrested growth of the enveloping membranes. Such arrests preceded development of ocular, cardiac and other abnormalities of the embryo. Moreover, Mall[16] (1908), after a lifetime investigation of the subject, concluded that faulty placentation — as manifested, for example, in ectopic pregnancy — was the most important causative factor of acquired maldevelopment in human embryos.

Though placenta previa, placenta accreta, circumvallate placenta and velamentous insertion of the cord were each found only once, the collective finding is provocative. It is reasonable to infer that cases of ante-partum bleeding also represented similar specific placental disorders. The association of placenta previa with ante-partum bleeding and an increased incidence of fetal defects has been established by many investigations.[5, 17] According to Irving,[18] placenta accreta probably results from an imperfect development of the decidua, and "as in placenta previa the frequent bearing of children seems to be an etiologic factor." Williams[19] describes the velamentous insertion of the cord as occurring "comparatively often (9 twins to 1 single) in twin pregnancy, and in single ovum twins is supposed to play a part in the production of hydramnios." Of 47 cases of circumvallate placenta studied by Hunt and his co-workers,[20] 15 were characterized by free or spotty vaginal bleeding or drainage of amniotic fluid before the fourth month of gestation.

TABLE 4. *Esophageal Atresia and Placental Conditions in 29 Pregnancies.*

CONDITION	RATE PER 1000 LIVE BIRTHS		
	CASES	OBSERVED	EXPECTED*
Hydramnion	20	230	2.5
Ante-partum vaginal hemorrhage†	6	69	—
Twin placenta	4	46	10.6
Placenta previa	1	11.4	5.5
Placenta accreta	1	11.4	0.25
Placenta circumvallata	1	11.4	5.30
Placenta velamentosa	1	11.4	8.40

*Figures from various sources.[5, 17-20]

†Defined as "staining into the 2nd month," "at 1-2 months," "until 6 months," "at the 6th or 7th weeks," "at the 8th month — considerable," and "for the first 3 months."

Fetal mortality was 50 per cent. The authors believe the placenta becomes cup-shaped because of early degenerative changes along the border that interfere with the blood supply of the fetus. In compensation, villi grow beneath and beyond the fibrous limit of the frondosum and are covered by the chorionic membrane. The heaped-up villi surround the margin of the placenta until increasing tension causes tears, bleeding or seepage of amniotic fluid. Unquestionably, such placental diseases could affect the nutrition or oxygenation of the fetus although it is impossible to estimate the role played by each of the multiple factors possibly involved,[21] such as anoxia and vitamin deficiencies.[22]

EMBRYOLOGY†

Fully 90 per cent of the cases under discussion present a single, definite pattern. There is a per-

*Reported by permission of Dr. Johannes Ipsen.

†We are indebted to Dr. F. T. Lewis, of the Department of Anatomy, Harvard Medical School, for the preparation of this section and permission to use Figure 4.

sistent communication between the trachea, near its bifurcation, and the esophagus, and just above this fistula there is a transverse division of the esophagus that is abnormal at any stage of development. An embryologic interpretation of this combination is all that can be attempted here. Apparently, the first case of the anomaly to be reported in a young embryo was found in what Minot[23] regarded as

FIGURE 3. *Sagittal Section of a Human Embryo of 18.1 mm., with Atresia of the Esophagus and Tracheoesophageal Fistula. The full length of the blind upper segment of the esophagus is not included, but the portion of the trachea from its fistula to the bronchial bifurcation is shown. The lower segment of the esophagus, in a fusiform dilatation, passes out of the section before reaching the diaphragm. (Harvard Embryological Collection, Series 1129, Section 171.)*

a normal specimen of 18.1 mm., with an estimated age of forty days. At that stage the abnormality was as fully established as at birth (Fig. 3), and the writer who discovered it sought its explanation in much younger embryos.[24]

Broman,[25] in his monograph on the development of the omental bursa, had reported that in human embryos of 3.4 mm., the common cleft-like cavity that later becomes vertically subdivided into the ventral trachea and the dorsal esophagus is closely flanked on either side by similar extensions of the peritoneal cavities. These extensions he named significantly the right and left "*pneumatoenteric recesses*," but without recognizing their possible relation to the fistula and atresia. Any fluid that they contain would be separated from that within the amnion and within the yolk sac, but at that stage it would not be separated from subplacental fluid within the chorion. By connection with the pericardial cavity the contents of the recesses might be subject to pressure changes as the heart filled and emptied. Compression of the foregut between the recesses could divide the esophagus along their dorsal borders and produce the characteristic anomaly under discussion. They change in form rapidly, as the left one disappears and the right gives rise to the superior recess of the omental bursa. In an older embryo, which still measured only 3 mm., Broman has shown the anterior ends of these recesses crossing the esophagus, and yet already below the site of the anomaly.

An embryo of 4 mm., figured as a whole by Bremer,[26] who clearly reconstructed most of its

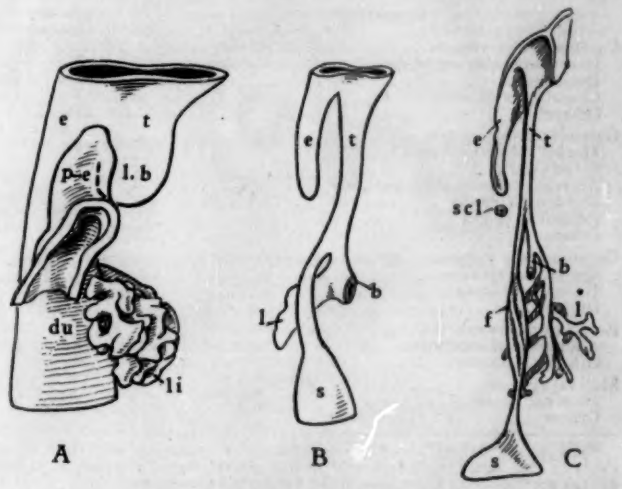

FIGURE 4. *Semischematic Lateral Views of Models of Human Embryos, Showing the Development of the Anomaly.*

A — *4.0-mm. normal (?) embryo modeled by F. T. Lewis;* B — *normal 8-mm. stage (Broman[25]), with the anomaly added; and* C — *the 18.1-mm. specimen (Fig. 3) modeled by Dr. Albert F. Boretti. In* A *the esophagus* (e) *is still undivided from the trachea* (t), *to which the pyriform lung bud* (l.b) *is appended.* P-e *demonstrates the right member of the paired pneumatoenteric recesses, undue pressure in which may produce the anomaly.* du = *duodenum.* li = *liver. In* B, e = *upper segment of the esophagus,* t = *trachea,* b = *right bronchus,* l = *left lung, and* s = *stomach. In* C, *as in* B, *with* scl, *where the anomalous right subclavian artery arises,* f = *a fusiform dilatation of the lower segment of the esophagus, above the collapsed stomach* (s).

organs, is used in Figure 4*A* to show how the associated atresia and fistula presumably arise. Malformation of the pneumatoenteric recesses, perhaps with undue pressure from their contents, in a brief period toward the close of the first month, could produce it. At 8 mm. it should be well established (Fig. 4*B*). In a misshapen 8-mm. thoracopagus Ysander[27] has figured mirror-image cases, one in each thorax of the double monster, but since the "bronchi show repeated branching," the specimen is surely stunted. The general relations in

our 18.1-mm. specimen are shown in Figure 4*C*: a very similar 19-mm. anomaly has been described by Gladstone.[28]

Formerly, the anomalous occlusion of the human esophagus was ascribed to pressure from the neighboring arteries. The dorsal aortas, converging to join behind the intestinal tract, meet at first at too low a level to obstruct the esophagus (a comparison with the description of Congdon[29] is of interest). Later, as the lengthening trachea and esophagus push down through their vascular encirclement, the fork formed by the junction of the two dorsal aortas comes to lie in the gap between the upper and lower segments of the anomalous esophagus. There, free from the resistance usually encountered, it has a marked tendency to persist as the "low origin of the right subclavian artery." Often, it is associated with other anomalies of the arterial trunks, especially of the vertebral arteries (as in the 18.1-mm. specimen), which may well affect the general nutrition of the fetus.

TABLE 5. *Number of Synchronisms Observed among 55 Infants with Tracheoesophageal Fistula.*

CONDITION	No. of CASES	
Cardiovascular system		38
Interventricular septal defect	8	
Dextroaorta	4	
Coarctation of aorta	3	
Others*	23	
Gastrointestinal system		53
Meckel's diverticulum	11	
Atresia ani	7	
Aberrant or anomalous pancreas	6	
Duodenal stenosis	4	
Persistent cloaca	2	
Others	23	
Genitourinary system		35
Ureteral dysplasias	6	
Horseshoe kidney	5	
Others	24	
Respiratory system		10
Anomalies of lobulation	8	
Others	2	
Skeletal system		9
Hemivertebrae	6	
Others	3	

*The term "others" includes abnormalities occurring less than three times in this series, and does not include patent foramen ovale or patent ductus arteriosus as anomalies of the cardiovascular system.

Two other consequences of the early transection of the esophagus may be expected—one occasionally and the other frequently. Normally, although the digestive tube is elsewhere pervious throughout, its lumen is temporarily interrupted by epithelial septums in the duodenum, and the anus is imperforate. These occlusions, both of which are present though not yet abnormal in the 18.1-mm. specimen, tend to persist. The anal opening should form in embryos of the ninth week (22 to 30 mm.), but for some reason still unknown the imperforate condition can persist, and it does so especially in association with an earlier interrupted esophagus.

TERATOLOGY

Coexisting anomalies that are prominent in the syndrome of esophageal atresia and TEF (Table 5) involve entodermal and mesodermal derivatives actively differentiating during the first half of the second month of embryonic life when the trachea and esophagus are also undergoing rapid development. The significance of such defects may be evaluated in comparison with expected embryologic sequences (Table 6).

Autopsies performed on 70 infants revealed all but 3 to have TEF. Fifty-five had a total of 145 coexisting defects as shown in Table 5, such as dextroaorta, coarctation of the aorta, Meckel's diverticulum, atresia ani, horseshoe kidney and vertebral dysplasias. The findings confirm a previous study of Ipsen and Okkels,[33] who made the reasonable inference that such recurring anomalies originate around the same time as TEF. They reported autopsies of 5 infants with TEF and compared findings of 30 published cases. Over three fourths showed other associated malformations, which the authors called synchronisms; most common were atresia ani and defects in development of the urogenital tubercle, of the hand or of the heart and great vessels. They traced the stages by which the trachea normally develops and differentiates from the esophageal primordium in relation to growth (crown-rump length) of the embryo and discussed the significance of synchronisms as a means of establishing the time of developmental arrest. For example, the coexistence of atresia ani and rectovaginal fistula with TEF was interpreted as a manifestation of synchronous arrests of development about the sixth week of fetal life, before perforation of the anal membrane had taken place and before completion of the partition between the rectum and urogenital sinus.

Although simple arrest of differentiation may serve to explain some of the anomalies listed in Table 6 (such as imperforate anus), additional ablation or dissociation* of the entodermal tissues is necessarily postulated to account for other types (for example, transverse division of the esophagus), which have no counterpart in the normally developing embryo. Proof exists (Figure 3) that TEF may be present as early as the 18.1-mm — or second-month—stage of life; and whatever the mechanisms of pathogenesis, the kinds of anomaly listed in Table 6 suggest the need for clinical study of the events of early pregnancy in the search for causative factors.

DISCUSSION

The nature of both the primary anomaly and the associated defects shows that TEF is determined long before birth, and proof exists that the defect may be present as early as the second month (2.5-mm. to 25.0-mm. stage) of embryonic life. Whether the malformation is of genetic or acquired origin is the first problem to be decided.

*This term is defined as follows by Mall[34]: "The repair of a simple wound in the embryo is always associated with further development of the surrounding parts, and in case the process ends in a perfect result normal development still remains, with or without regeneration. When, however, the embryonic tissues become mixed. . . we have a new condition quite unlike any pathological change found in the adult. This pathological condition I shall term dissociation."

In the combined series of Plass[2] and ourselves TEF was never recorded as having appeared in successive generations or recurring in the same generations of 243 families. Although the possibility of a genetic origin is not disproved by negative findings, the positive teratologic observations of this study permit the formulation of an alternative hypothesis. On the basis of the morphology of the tracheoesophageal defect and that of associated arrests (Table 5), the syndrome is postulated as acquired during early fetal life — with departure from normal sequences of development (Table 6) occurring at about the fifth or sixth week. If this interpretation is correct the biologic pattern of TEF is analogous to that previously described for mongolism[35] except for basic differences in the stages and organs involved by disease.

The principle that a specific agent acting on the embryo may give rise to widely divergent teratologic manifestations in human beings[36] as well as animals[15, 22, 37] has been amply confirmed by observations that numerous cardiac, dental and cerebral synchronisms characterize the syndrome of post-rubella congenital cataract.[38] The facts pertinent to mongolism were interpreted to indicate that a specific clinical defect may be engendered by multiple unrelated agents, and that the particular result was a nonspecific function of the stage (eighth week) of embryonic development — not a specific property of the agent. Although the epidemiologic findings on which the inference rests await confirmation by others, the biologic principle postulated has been conclusively established for the better part of a century by investigators in the field of experimental zoology.[15, 37] The teratologic findings in the present study imply that TEF also is a function of host development, for all the recurring synchronisms involve entodermal or mesodermal structures differentiating at the fifth or sixth week of embryonic life.

The lacking evidence necessary to prove a hypothesis that TEF and its synchronisms represent departures from normal development during the early part of the second month of embryonic life caused by agents acting through the mother and placenta relates to their specific identification and demonstration of activity at this period. The kinds of agent to be considered and tested as possible causes of prenatal disease of the conceptus have been the subject of study by Ingalls and Gordon.[21] Agents were grouped in three categories: infectious (rubella, syphilis), chemical (nutritional deficiencies, toxic and metabolic disturbances) and physical (mechanical trauma, structural disease of the uterus). A relatively high incidence of maternal illegitimacy observed in this series, if confirmed, would suggest an occasional connection with attempted abortion — with the agent either mechanical or chemical (quinine in Case 10). A possible connection with spontaneous threatened abortion

TABLE 6. *Physiologic Events Pertinent to Tracheoesophageal Fistula (Fourth to Eighth Weeks of Fetal Life).**

WEEK	RESPIRATORY SYSTEM	GASTROINTESTINAL SYSTEM	CARDIOVASCULAR SYSTEM	GENITOURINARY SYSTEM	SKELETAL SYSTEM
4th (0.5–2.5 mm.)	Tracheal primordium buds off ventral esophagus, and longitudinal grooves appear	The pharynx, foregut, hindgut, and cloaca comprise the gastrointestinal tract sealed at either end by the pharyngeal and cloacal membranes	Paired aortas with dorsal and ventral components have differentiated from primitive capillary networks; heart has become a single tube with atrium, ventricle and bulb.	Condensations of mesenchyme form mesonephros, with imperforate duct reaching to cloaca	Sclerotomes formed by condensations of mesenchyme about chorda
5th (2.6–5.5 mm.)	Pharyngeal membrane ruptures; beginning separation of trachea from esophagus from below upward; lung bud appears.	Yolk sac separates; double primordium of pancreas buds from duodenum; cloaca differentiates into anus and urogenital sinus.	Primordia of semilunar valves, septum primum and septum secundum are evident; cardiac chambers intercommunicate freely.	Mesonephric ducts develop lumen, the primordia of primitive pelves and ureters	Vertebral cartilages on left side are separated from those of the right by the pericordal septum; chondrification of limbs begins.
6th (5.6–11 mm.)	Further lobulation of lungs and formation of bronchi; definitive separation of trachea from esophagus occurs.	Involution of yolk sac; two pancreatic primordia approach each other; partitioning of rectum from urogenital sinus completed.	Primordia of cardiac septums develop as heart bends and rotates to right; fourth left aortic arch emerges as dominant great vessel; descending aortas fuse from 7th intersegmental arteries to bifurcation.	Primitive kidneys differentiate close together in urogenital folds below aortic bifurcation; ureters elongate and pelves migrate cephalad toward nephrogenic tissues.	Perichordal septum is broken through by hyaline cartilage, which unites about chorda; carpal and tarsal chondrifications are evident.
7th (12–17 mm.)	Septum between trachea and esophagus has been completed; both structures elongate.	Fusion of pancreatic primordia results in formation of single organ; rectum has developed and anal membrane is present.	Duplication of wall between cardiac limbs lags in development resulting in 3 chambers: sinus venosum, atrium and ventricle.	Differentiation of calyxes and integration of collecting tubules with primitive secretory and vascular units	Articular and laminar processes of vertebras develop; first row of phalanges has differentiated.
8th (18–25 mm.)	Lung development continues coincidentally with bronchial differentiation	Yolk sac has atrophied; dorsal pancreatic duct disappears and duct of Wirsung develops; rupture of anal membrane occurs.	Subdivisioning of heart; development of valvular apparatus; and contours of great vessels largely established.	Further differentiation, migration and rotation of kidneys	Further differentiation of cartilaginous skeleton and beginning ossification of previously formed structures

*Sources of data: Dodds,[30] Keibel, F., and Mall[31] and Arey.[32]

(and the agents that produce it) is suggested by the finding that 6 of 29 mothers had ante-partum vaginal bleeding. Five of these 6 bled during the first trimester of pregnancy. That infectious agents are involved in some cases is suggested by the fact that 5 of the 6 cases of acute illness were localized in early pregnancy instead of being scattered throughout. Such evidence is necessarily fragmentary and inconclusive, for TEF occurs rarely, 100 cases such as those assembled here representing the product of about half a million births. The future investigation of such a rare condition lies with the large lying-in hospital. If the mother's prenatal course has not been recorded in satisfactory detail it should be reviewed immediately after the baby is born — before the events of early pregnancy are no longer accessible. We hope that this article will prompt physicians to record and publish further data by which the hypothesis set forward here can be either confirmed or discarded. The question at issue is not merely the etiology of a rare syndrome but also principles underlying cause and prevention of all malformations acquired during prenatal life.[21] It is likewise increasingly evident that the basic problem is not clinical, embryologic, bacteriologic, biochemical or genetic, but an aggregate of those disciplines, which includes also application of epidemiologic and statistical methods.

Summary

The causative agents of congenital atresia of the esophagus must be primarily genetic or else acquired during prenatal life because the defect is present at birth. A review of the records of 107 infants with the condition revealed no case in which the defect appeared in successive generations or recurred in the same generations of a family; 102 of the infants had an associated tracheoesophageal fistula (TEF) and significant associations were also observed with anomalies of the cardiovascular, gastrointestinal, genitourinary, respiratory and skeletal systems. On the basis of the morphology of the tracheoesophageal defect and that of associated arrests the syndrome is postulated as acquired during early fetal life—with departures from normal sequences of development occurring at about the fifth or sixth week. If this interpretation is correct the biologic pattern of TEF is analogous to that previously described for mongolism except for basic differences in the stages and organs involved by disease.

A study of maternal factors confirmed previous observations of a significant association with hydramnios. Twins were encountered in 4 cases; 6 mothers had ante-partum hemorrhage (5 in the first or second month), and 6 also suffered acute infections or metabolic disturbances in the first trimester of pregnancy.

The hypothesis is made that esophageal atresia, tracheoesophageal fistula and certain commonly associated defects represent departures from normal development about the fifth or sixth week of embryonic life caused by agents acting through the mother and placenta. This hypothesis should be tested by future observations since the question at issue not only is one of specific etiology but also involves principles underlying the larger phenomenon of acquired congenital malformations.

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DEATH DUE TO CARDIAC DISEASE FOLLOWING THE USE OF EMETINE HYDROCHLORIDE IN CONDITIONED-REFLEX TREATMENT OF CHRONIC ALCOHOLISM

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BECAUSE of the increasing use of emetine hydrochloride in the conditioned-reflex treatment of chronic alcoholism, because the cardiac manifestations of toxicity have not been stressed in the literature and because deaths can probably be avoided by consideration of certain gastrointestinal and neuromuscular warning symptoms of toxicity, the following fatal case of myocardial damage after emetine administration is being reported.

CASE REPORT

A 33-year-old man was first seen on November 10, 1947, at 11 p.m., 1 week after his last of a series of ten emetine injections for conditioned-reflex treatment of chronic alcoholism at a nearby mental institution. His complaints were weakness, dyspnea, tachycardia and nausea of 1 week's duration. The schedule of treatment had been 0.06 gm. (1.0 gr.) of emetine hydrochloride intramuscularly for 4 consecutive days, followed by a rest of 1 day and then 0.09 gm. (1.5 gr.) for 5 consecutive days and ending with an injection of 0.06 gm. on November 1, making a total of 0.75 gm. (12.5 gr.). Diarrhea, which had begun after the fifth injection, had stopped 2 days previously. In addition to the diarrhea, there had been fatigue, dyspnea, weakness and trembling. In spite of a pounding rapid heart rate, treatment with emetine was continued, the symptoms being ascribed to the patient's nervousness and emotional state. No electrocardiograms were taken before or after treatment.

He had been seen on numerous occasions from 1939 through 1945, in which year, on April 28, no evidence of cardiac damage had been found.

On physical examination he appeared acutely ill, with pallor, slight cyanosis, increased respirations, tachycardia (rate of 140), with marked gallop rhythm, a blood pressure of 70/60, an engorged liver and lungs and hyperactive reflexes. He was immediately hospitalized and given oxygen, 50 per cent glucose, sedation and a salt-free diet. Laboratory examination showed a normal urine with good concentration. Examination of the blood disclosed a red-cell count of 5,150,000, with a hemoglobin of 20.3 gm. The nonprotein nitrogen was 60 mg. per 100 cc., and the vital capacity 3.8 liters. The circulation time by the magnesium sulfate method was 25 seconds, and the venous pressure was equivalent to 14 cm. of water. An x-ray film of the chest demonstrated the heart to be enlarged with marked congestion extending from both hilar areas, particularly on the right, but with no fluid in either pleural cavity. The electrocardiographic tracings (Fig. 1) were interpreted as showing sinus tachycardia (rate of 150) with a PR interval of 0.2 and QRS complex of 0.06 second, inverted T waves in all leads, elevated ST segments in Leads V_2, V_3 and V_4 and low R waves and deep S waves in Leads V_1, V_2, V_3 and V_4. The tracing was regarded as consistent with extensive myocardial damage.

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On the following morning Dr. S. A. Levine found a marked gallop rhythm and a regular apical rate of 140, which slowed smoothly with carotid pressure. He agreed with the diagnosis of toxic myocarditis due to emetine and advised 50 mg. of thiamine chloride intramuscularly, salt-free diet, fluids ad libitum, 50 cc. of 50 per cent glucose and digitalis for a dilated heart.

By 5 p.m. that afternoon the lungs had cleared, and the blood pressure was 80/60; the patient still complained of marked dyspnea in spite of 100 per cent oxygen inhalation.

The next morning the skin was moist, and he showed signs of peripheral shock. He was given plasma, 50 per cent glucose and sodium luminal intramuscularly. By 5 p.m. no pulse could be obtained, his veins were collapsed, and his chest was filling with rales. He died at 11:55 p.m., 48 hours after admission.

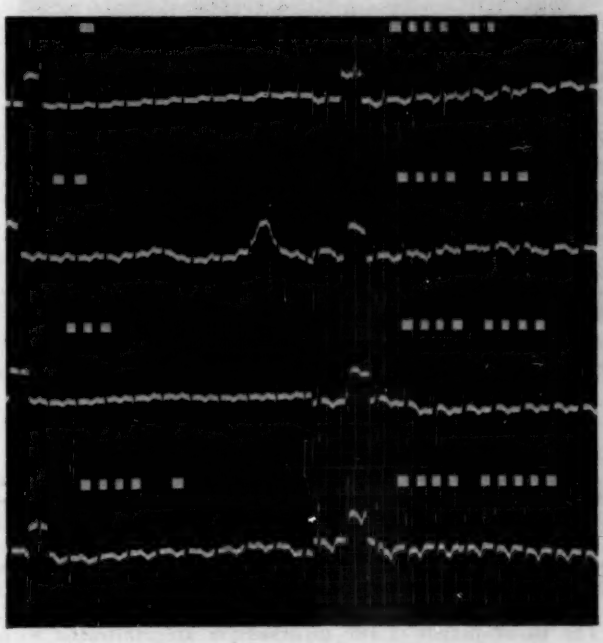

FIGURE 1. *Electrocardiographic Tracings.*

Autopsy findings were reported as follows by Dr. David Skinner:

> The positive findings are confined to the cardiovascular system, except for moderate dilatation of the stomach and slight fatty degeneration and focal necrosis of the liver.

The heart is moderately enlarged, globular and extremely soft and flabby. It measures 15 by 13 by 6 cm. and weighs 450 gm. The epicardial surface is slightly dull and presents a few dark-crimson petechiae, particularly on the posterior surface. There is a moderate amount of subepicardial fat. The myocardium is soft, flabby and light red brown. The endocardium is smooth and glistening. The coronary arteries are soft and patent. There is minimal fusion of the commissures of the cusps of the aortic valve, with slight thickening of the cusps near the commissures. Histologic sections of the heart show the pericardium at points to be covered with fairly old, unorganized fibrin. The underlying pericardium contains diffuse and focal infiltrations of moderate numbers of lymphocytes, histiocytes and plasma cells. At points in the pericardium are small foci of extravasated erythrocytes accompanied by a small number of neutrophils. The myocardium throughout is slightly edematous, and large numbers of muscle cells contain minute fat vacuoles. Occasional muscle cells are undergoing ischemic necrosis and are being infiltrated with histiocytes, lymphocytes or rarely by neutrophils. The tissue planes of the myocardium are infiltrated with small numbers of lymphocytes, histiocytes and rare plasma cells and eosinophils; this cellular infiltration is more marked in the right ventricle than in the left (Fig. 2). Sections of the anterior descending coronary artery show a slight intimal fibrosis, with a very small amount of atheromatous debris. Sections of the conduction system are not remarkable.

FIGURE 2. *Section of the Apical Portion of the Right Ventricle (Phloxine and Methylene Blue Stain x 133).*

There is marked acute passive congestion of the liver, spleen, kidneys and intestine. There is moderate cerebral congestion and edema and slight passive congestion and edema. Each pleural cavity contains approximately 400 cc. of clear fluid.

The final diagnoses were: toxic myocarditis, chronic fibrinous pericarditis with petechiae, chronic myocarditis with focal necrosis, fatty degeneration and edema of the myocardium, cardiovascular collapse (shock and decompensation), pulmonary congestion and edema, slight, marked passive congestion of the liver, spleen, kidneys and intestine, moderate cerebral congestion and edema, bilateral hydrothorax, slight retroperitoneal edema, focal necrosis and fatty degeneration of the liver, dilatation of the stomach, calcified mesenteric lymph node, slight aortic atherosclerosis and old, healed appendectomy scar.

DISCUSSION

In 1948 O'Hallaren and Lemere[1] reported 2323 cases of conditioned-reflex treatment of chronic alcoholism with emetine without a warning of the dangers to the heart. They state that "the treatment is a safe procedure if administered by properly trained personnel." They report 3 deaths, 1 from congestive heart failure and 2 from coronary occlusion. They present no program to prevent such a tragedy as is reported above. The safety of this procedure could be increased if the properly trained personnel is on the alert for signs of cardiac toxicity.

In 1947 Dack and Moloshok[2] brought the literature up to date but reported no deaths specifically cardiac in origin. Six deaths were described as occurring after a total of only 0.6 gm. (10 gr.), but the majority followed 1.2 gm. (20 gr.) or more. The patient in the case reported below received 0.75 gm. (12.5 gr.) hypodermically, in addition to a small amount by mouth several minutes prior to vomiting.

Electrocardiographic changes after administration have been reported as follows: ventricular fibrillation (in rabbits)[3]; intraventricular block, inversion of T waves and cardiac arrythmias (in experimental intoxication in cats)[4]; T-wave depressions in all leads, chiefly in the limb leads in man[5]; a T wave of the coronary type in Lead 4, with precordial pain persisting for about an hour in man[5]; auricular fibrillation after six daily injections of 0.02 gm. (⅓ gr.) in man[6]; ventricular tachycardia and finally ventricular fibrillation in rabbits — the minimal intravenous lethal dose in these animals is about 2 mg. per pound of body weight[7]; increase in auriculoventricular conduction in man[5]; and premature systoles, both auricular and ventricular but ventricular predominantly in man.[5]

These changes are evidently reversible if the subject survives. Berman and Leake[7] found no marked permanent changes in tracings after daily intravenous injections approximately equivalent to 1 mg. per pound of body weight in rabbits.

Boyd and Scherf[4] observed that electrocardiographic alterations gradually disappear within forty-five minutes in dogs. However, Klatskin and Friedman[8] and Dack and Moloshok[2] reported that in man abnormalities persisted for two months or more.

Though most of the experimental investigation has been in animals, several writers have studied the cardiologic effects of emetine in patients with amebic dysentery treated with the drug. Hardgrove and Smith[9] studied 72 patients with dysentery in the Canal Zone receiving 0.6 gm. of the

drug in ten days. They found minor electrocardiographic changes in 52.7 per cent but concluded that with these doses emetine is not dangerous — though electrocardiographic studies should be made before, during and after treatment. The delayed appearance of electrocardiographic abnormalities must be stressed. Dack and Moloshok[2] described changes often delayed until one or two weeks after discontinuation of the treatment as in the case reported above. They conclude that absence of electrocardiographic changes during treatment does not warrant continuing the drug beyond a certain dose. Klatskin and Friedman[8] concluded that toxic manifestations may occur at any level of dosage depending on individual susceptibility to the drug. They found that the drug is cumulative in the myocardium and that rest periods between courses of the drug should therefore be adequate.

Rinehart and Anderson[9] have studied the effect of emetine on cardiac muscle in rabbits. They found lesions similar to the Aschoff reaction of acute rheumatic fever. The changes were both acute and chronic. The former consisted of interstitial edema of the muscle, and the latter of necrosis of fibers and degenerative swelling. Focal proliferation of interstitial tissue resulted in response to necrosis of muscle fibers. Lymphocytes, plasma cells, eosinophils and polymorphonuclear neutrophils were found in such foci. Nuclei of muscle fibers showed changes in size and distribution of chromatin interpreted as evidence of injury. Small cellular scars about necrotic muscle fibers were found in chronic intoxication. The lesions were of distinctly greater severity in the heart than in skeletal muscle or liver.

There is no known specific treatment for the cardiac damage due to emetine. One is left with symptomatic management and the usual measures for the handling of cardiac failure, which include rest, sedation, plasma, oxygen, salt-free diet and the judicious use of digitalis and quinidine. Prevention is all important. It is suggested that rules be set up to govern all patients being given conditioned-reflex treatment for alcoholism by means of emetine. Experience of others and the lack of cardiac supervision of this case during treatment suggest the following rules as minimum requirements: an electrocardiogram should be taken before, during and one or two weeks after treatment; suspected organic heart disease should contraindicate treatment; the total dose of emetine should not exceed 0.6 gm. (10 gr.) in any one course; at least two months should elapse between courses of treatment in patients who show any electrocardiographic changes during treatment; when significant electrocardiographic changes occur, treatment should be stopped at once; and signs of toxicity — namely, diarrhea, fatigue, dyspnea, muscular tremors or weakness — and dizziness should be carefully watched for daily, and if these develop the heart should be watched with great care (an increasing tachycardia with the patient at rest calls for at least temporary cessation of treatment).

The prognosis in these cases is good if the early signs of cardiac damage have been heeded, since the pathologic process is reversible.

Summary

A death apparently due to the toxic action of emetine on the myocardium is reported. The drug was used in the conditioned-reflex treatment of chronic alcoholism in a healthy young man.

A program designed to prevent a recurrence of such a tragedy is suggested.

A dosage limit of 0.6 gm. (10 gr.) in any one course should not be exceeded.

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MEDICAL CARE FOR THE AMERICAN PEOPLE*

Is Compulsory Health Insurance the Solution?

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MR. OSCAR R. EWING, Federal Security Administrator, in his report to the President[1] urges compulsory Government health insurance as an essential part of a long-range program to improve the health of the nation. He points out that the 5,000,000 men rejected by the draft as unfit for the armed forces, the 4,300,000 man years of work lost through bad health and the national loss of $27,000,000 in national wealth through sickness and partial and total disability are evidences of the bad state of the national health, and that at least 70,000,000 people in this country will have difficulty in providing adequate minimal medical care for themselves and their families.

How do these more prominent reasons for the establishment of a federal insurance program stand up under factual analysis? Is there a real need for such a program? If not, what are the more important reasons for opposing it at this time?

Will Compulsory Health Insurance Improve the Nation's Health?

We, as physicians, recognize the need for continually improving the many factors that contribute to better health. But are we, and is the public, properly informed when we are told that the way to better health is through compulsory health insurance? The following quotation from Simons and Sinai[2] is most instructive:

> When insurance systems are being urged upon governments, one of the strongest arguments offered is that improvement in general health will follow prompt, universal medical care. After the system has been adopted, one of the most amazing things to the outside observer is the almost complete absence in the vast amount of discussion of any reference to public health in relation to insurance. Moreover, not even the most intense partisan of insurance has ever attempted to present any statistical proof that insurance has any effect upon the general death- and sickness-rate. No sort of statistical manipulation has ever been able to show any correlation between the movements of death-rate in insurance and non-insurance countries. They have declined in both at about equal rate, according to sanitary and health measures and other influences; but no difference in any way traceable to insurance can be discovered.
>
> This is the more remarkable since water protection, better housing, tuberculosis care, isolation, immunization, and numerous other health measures do show such traceable results. At no point has a disappointment been greater than in the failure of insurance as a preventive measure.
>
> Contrary to all prediction, the most startling fact about the vital statistics of insurance countries is the steady and fairly rapid rate of increase in the number of days the average person is sick annually and the continuously increasing duration of such sickness.

The average recorded sickness for each person per year practically doubled in Great Britain and Germany after the installation of Government insurance.[2] What evidence does Mr. Ewing have to suggest that the effect of Government insurance upon work days lost through sickness will be any different in this country than in others?

We still read that the high percentage of rejections in the military recruitment program has provided striking evidence of the unsatisfactory state of the nation's health and that for this reason a national health insurance program is essential. We, as physicians, know that there are millions of men in this country in good health who will not meet the rigid requirements for combat duty in the armed forces. We know that at least 80 per cent of those rejected could not have been rehabilitated by any medical care known at this time, and we know that of the approximately 20 per cent who might have been influenced by medical care, it would have been necessary for them to have consulted the doctor, to have accepted his recommendation and for the treatment to have been completely successful.[3]

We, as a profession, are the first to recognize the importance of improved sanitation and other public-health measures. They are fundamental to any program to improve the nation's health, but provision of these is in no way dependent upon or to be confused with a compulsory health insurance program.

Is Compulsory Health Insurance Necessary to Provide Medical Care to Half the Population?

What are the facts concerning the "70,000,000 people" who "will have difficulty in providing adequate minimal care for themselves and their families"?

About 28 per cent of the families of this country had incomes under $2000 in 1946.[4] Many of these can pay nothing or only a portion of the cost of a serious illness. The indigent are provided for in the present Administration bill (S 5) only when "equitable reimbursements to the account on behalf of such needy or other individuals have been made, or for which reasonable assurance of such reimbursements has been given, by public agencies of the United States, the several states" and so forth. The same agencies could readily purchase such care

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from medical care programs already in existence or in process of formation. There is, then, no need for a compulsory Government health insurance agency to assure proper care for this group.

Approximately 50 per cent of our families are now earning between $2000 and $5000 a year. Good medical care is and will remain costly. The total expenses associated with a serious illness are too high for most of these families to meet without difficulty at the time of the sickness. However, many own automobiles, television sets and electric refrigerators, and, as a group, they spend a large amount on alcoholic beverages and other things. These are accepted as a part of the American life. But, at the same time, if these families had to pay cash for their automobiles, for their electric refrigerators or for their television or radio sets, many would not be in a position to buy them. Is it fair to say that because they cannot pay cash for these items, they cannot afford them? Because this same group cannot pay for a major illness at the time it occurs, is it just to assume that they cannot afford to pay for it? Because a mechanism to spread the costs of serious illness must be made available to these families, why must it be done under the costly, inflexible and inefficient machinery of federal Government before thorough exploration of reasonable alternatives?

We need have no great concern for those with incomes over $5000, although we must also accept the fact that it is customary for most of us to adjust our standards of living pretty well to our incomes, to the end that many families with annual incomes between $5000 and $10,000 will have difficulty in paying large medical bills at the time at which they are incurred. Many of these recognize the importance of spreading the cost of illness, and for them such a mechanism would be a convenience though not a necessity.

We have now in this country the highest quality of medical care, the best teaching and the most productive research of any country anywhere. As the science of medicine has improved to make this possible, the costs have increased. We have not developed a satisfactory means of paying these increased costs. Industry was faced with, and successfully met, a similar problem in selling its technical products. Because we as a profession have failed to lead the way, we as a nation are now being urged to make a complete change from a system of medical practice that places emphasis on quality of service and direct responsibility to the individual and his family, to a system that had its concept in the Bismarckian philosophy, which puts emphasis on quantity rather than quality, and which fixes the ultimate responsibility of the physician to the central Government rather than to the patient.

We are unable to find any factual evidence to support the contention that compulsory health insurance will improve the health of the nation. A sound program to afford medical care to the needy is not dependent upon a Government insurance system. There is urgent need for developing a method of paying for the medical care of the large segment of our population who cannot, or would prefer not to, meet the payment for serious illness when it comes. Does our failure to have provided a mechanism for doing this justify a complete change from any possible solution of this problem on a voluntary basis to a system of compulsion that has been tried in so many foreign countries and has as yet provided no country with the quality of medical care equal to ours?

Does Compulsory Health Insurance Meet the Qualifications of a Good Medical Care Plan?

Without careful analysis it might seem very reasonable for all of us to pay a tax to the federal Government, which, in turn, takes the responsibility of supplying us with and paying for our medical care whenever we need it. It is a very easy matter, in writing, from the platform or over the air, to develop a logical and apparently practical program. It must be remembered, however, that a successful program to provide prepaid medical care is dependent upon certain fundamental principles. The more important of these are: free choice of physician; mutual co-operation of the public, those rendering professional services and the administrative agencies; continuing improvement in the quality of care given, the teaching in medical schools and research; and a total cost of the program in keeping with the general economy of the community.

Free choice of physician. Only a short time ago Mr. Ewing[5] assured the public that from the patient's point of view there was absolutely no difference between the present system and that which the Administration was proposing (compulsory health insurance) except that the Government would pay the bill. If this is true it means that you as a patient can go to any physician you wish at any time, provided he is available and is willing to accept you. At present he is limited in the number of patients he can care for only by the number who seek his services or by the number of working hours in his week. Since those who can are expected to pay for his services, he is spared a multitude of demands upon his time for minor, insignificant complaints. The fact that longer hours mean greater income is an incentive for him to be available to prospective patients throughout most of each twenty-four hours. Mr. Ewing knows and his advisers know that a medical care plan of the magnitude proposed cannot remain solvent if the physician is paid each time he sees a patient. They know that removal of any financial responsibility from the patient will greatly increase the demands upon the physician's time for unimportant complaints. They know that the number of patients a physician will

be permitted to care for must be limited. Every prospective patient in a community must register and have his name on some doctor's panel. The best known doctor in each community will be in the greatest demand, and in fairness to all, those first applying must be accepted until the panel is filled. When his panel is filled, all others desirous of being under his care must select another doctor or will be assigned to one by those responsible for carrying out the plan. Moreover, there will undoubtedly be a certain number of the most successful and older physicians in each area who may well prefer not to become part of such a program. Under compulsory health insurance the free choice of physician cannot be assured to anywhere near the degree that it is available at the present time.

Co-operation. Co-operation between those giving, those receiving and those administering any plan is essential. Co-operation means mutual confidence and mutual respect.

We hear Mr. Ewing[5] over the public radio say that there will be absolutely no change in the relationship between the patient and the doctor, except that the Government pays the bill, and that the maximum payment that anyone will have to meet is $1.40 per week. We know that it will be absolutely impossible to maintain, under a Government program, the private practice of medicine as it now exists. We know, and Mr. Ewing should know, that a maximum of $1.40 per week on the part of the worker, in addition to a like amount from the employer, cannot possibly support the comprehensive program outlined. Such statements are misleading and do not inspire the confidence of an enlightened public or of the medical profession.

Mr. Ewing[1] states that there are 325,000 lives lost in this country each year that we have the knowledge to save. We are not told the basis for these figures, but we read that 117,000 of these lives are lost through heart disease and cancer. We know that the death rate for heart disease among the physicians of the country is higher than it is in the population at large.[6] We do not believe that lack of medical care is responsible for the greater number of our profession who die each year of this condition, and therefore we fail to understand how a compulsory health insurance program will help save the lives of others who have heart disease. We know that in the state of Massachusetts only 0.3 per cent[7] of those coming to our cancer clinics have delayed in coming because of economic reasons. We do not know how to make an earlier diagnosis of cancer of the internal organs, many of which give symptoms too late for cure. We do not know how to remove from the patient the fear of reality, dread of an operation and other factors that postpone early diagnosis and treatment of cancer. We are certain that the introduction of a compulsory health insurance program will not alter these factors and therefore will have little effect upon the death rate from this disease.

We are, therefore, at a loss to understand the basis for Mr. Ewing's figures or how we, as a medical profession, can have confidence in an agency and its administrator that are responsible for giving to the public this kind of information. Nor do we understand how Mr. Ewing can have confidence in and co-operate with a profession of which he says, "Which is the more important? The personal, selfish business and professional values of 180,000 practicing physicians in this country, or the health and well-being of some 68,000,000 of our population?"[8]

Surely there is nothing in the material discussed above to assure the type of mutual confidence and respect that is essential to the smooth running of so important a program.

Quality of care. Whenever compulsory health coverage has been adopted, the emphasis has been on quantity and not on quality of care. This was so in Germany, was and is so in England, is so in New Zealand, and, if adopted, it will be so here. Unethical though it may be, it is common practice to get everything possible from anything as remote from the individual and as wealthy as a government. Seeing too many people with minor transient complaints and nothing wrong dulls the doctor's perception for the early signs of serious disease. History taking and examinations become superficial and a matter of routine.

Good medical care cannot be assured by legislation or by any mechanism of payment. It is personal, individual and intangible, and it depends not only on the training and experience of the physician, upon his scientific accomplishments and facilities but, more than anything else, upon the intensity and thoughtfulness with which he applies these to the individual patient who is sick. A feeling of responsibility directly to the patient and to his family, as well as ethical competition between physicians for the confidence of the public, is the more important factor in assuring each patient the personal care that he wants from his doctor. Any third party coming between the patient and his physician may interfere with this relationship, but when Government assumes complete responsibility for paying the physician and for providing medical care to the patient, such a relationship cannot survive.

It is difficult to foresee just how far reaching the effect of compulsory health insurance might be upon the actual care of the more complicated illnesses. What, if any, effect might it have upon the training of young men in preparation for the actual care of the sick? To those of us who are actively interested in preparing young men for the specialties, it is disturbing to learn that in New Zealand many desirable young doctors are not being attracted to the ranks of the future specialists and

teachers because the "unnaturally swollen rewards of general practice"[9] can be enjoyed after a much shorter and less arduous period of training than that necessary to qualify them for the all-important responsibilities of the specialists and of teaching.

The cost. Compulsory health insurance, as now advocated, is not insurance. There is no calculated risk, no payment of a premium to cover the cost of specific benefits and no contract. It is a form of taxation and should be recognized as such.

Comprehensive medical care is not an insurable risk. The demands upon such a program will be unlimited, indeterminate and uncontrollable. Abuse of the privileges is easy and attractive and therefore likely. The cost will be unpredictable and inordinately high.

In Berlin, the cost for sickness insurance almost doubled per member in the five years between 1925 and 1930,[10] resulting in the "Emergency Decree" of July, 1930. In New Zealand,[11] the total income from social-security taxes in 1945–1946 amounted to 15,000,000 pounds, and it was necessary to take 7,000,000 pounds from the consolidated fund to meet the total expenses of the social-security program. One year later, in the budget for 1946–1947, it was expected that 20,000,000 pounds would be received from the social-security taxes, owing to an increase in the rate. But during this year it was anticipated that 18,000,000 pounds, an amount almost equal to the total income of the social-security agency, would be taken from the consolidated fund to meet the expenses. This represents a social-security budget of 38,000,000 pounds, or 60 per cent of the revenue from all sources for the previous year.

In England, three months after the beginning of the present health program, Mr. Bevan made the following statement:

> Because things are free is no reason why people should abuse these opportunities. This is a great test of the maturity of the British people in so far as they have all of the resources of the medical profession at their disposal without charge. If any individual abuses the opportunity, he must reckon with a sum total which might add up to one too grievous to carry and for which it would be very difficult to continue to provide.

Two months before the end of the fiscal year the Ministry of Health asked for $233,820,000 in addition to the original estimate of $598,700,000 to meet the expenses of the program for the first nine months.[13]

We find little to comfort us in the report of the subcommittee of the Hoover Commission,[14] which studied the medical care program for which the Government is now responsible. The many evidences of extravagance and waste in money and in manpower are forcefully presented — for example, the Government pays $20,000 to $51,000 per bed for construction of hospitals in areas where voluntary hospitals are doing this for $16,000 per bed. In the New York area, hospitals contemplated or under construction will approximate a cost of $105,200,000, which the commission, after careful investigation, finds it difficult to justify. In Houston, Texas, the Veterans Administration is letting bids for a 1000-bed hospital at an estimated cost of $25,000,000, which the Commission believes would be unnecessary if the unoccupied beds in other governmental hospitals in that area were utilized. Evidence of the effect of the "free" hospital care of a Government-controlled program upon its cost is found in a comparison of the length of stay of patients after similar operations in voluntary and in Government hospitals (Table 1).

Not only is the actual cost for the care of each illness much greater in the Veterans Administration than in voluntary hospitals, but also the longer stay means that more beds are necessary to take care of the same number of patients. More beds means more construction, more personnel, more cost.

TABLE 1. *Average Hospital Stay in Voluntary and Government Hospitals.*

OPERATIVE PROCEDURE	AVERAGE HOSPITAL STAY	
	VOLUNTARY GENERAL HOSPITALS	VETERANS ADMINISTRATION HOSPITALS
	days	*days*
Appendectomy	7.8	14.3
Tonsillectomy	1.4	15.1
Hemorrhoidectomy	6.9	34.3
Herniotomy (inguinal)	10.3	27.0

The people of this country must realize that there is no such thing as mass production of medical services. Each examination, whether x-ray or clinical study of the patient, is a personal service and one that takes time, and will remain costly if well done, even under the most efficient type of program. Such a program as advocated by Mr. Ewing cannot possibly be paid for by payroll deduction but may necessitate a bottomless pit with limitless money. This can only mean a tax burden out of all proportion to the benefits received.

Free choice of physician, co-operation, continuing improvement in the quality of care given and a total cost in keeping with the local and national economy cannot be expected if compulsory health insurance is adopted. Because we believe these to be essential to a successful medical care plan, we are opposed to compulsory health insurance until sincere and co-ordinated efforts to attain these objectives by other means are made and found wanting.

Off with the Old, on with the New?

There are many who are very close to the problem of bringing good medical care to the American people who believe that a country so large and so diversified as ours may not lend itself to any single

over-all plan, that our objective should be to provide the most widespread distribution of the best available medical care at the lowest cost possible, that our planning should be concentrated upon the end rather than the means, and that only through programs carefully planned and efficiently administered will we later have the experience and background necessary to put into effect that program which most nearly meets these objectives. The adoption of compulsory health insurance would eliminate any possibility of experimentation outside the structure of the compulsory, centrally controlled plan. "Once the whole employed population, wives and children included, is brought within the scope of compulsory sickness insurance, the great majority of doctors, dentists, nurses, and hospitals find themselves engaged in the insurance medical service which squeezes out most of the private practice on the one hand, and most of the medical care heretofore given by public authorities on the other. The next step to a single national medical service is a short one."[15] Are we ready to discard completely the tremendous advances made by nonprofit and commercial agencies during the past ten years, or should our efforts be intensified to eliminate the many defects now recognized in present plans with the expectation that from these experiences will evolve a program that will be practical, effective, efficient and available to all who desire it?

Who Shall Be Our Keeper?

When we as a nation become dependent upon the Government for our medical care we come to think of the Government as a paternal agency to which we turn and upon which we become increasingly dependent. Bismarck recognized the importance of this when he put a compulsory health insurance program into effect in 1883. Since that time the adoption of a compulsory, Government-controlled medical care program has been one of the most important early steps in the more complete socialization of a country. This was so in Germany, and it is so in England and in New Zealand. If this is the will of the American people, it should be so here, but we should be remiss if we did not point out the implications of making the Government rather than ourselves responsible for anything so personal and so essential as medical care. We are told that this is not socialized medicine, that it is no different from "buying fire insurance" (Ewing). But when the Government takes complete responsibility for providing a service, when we are compelled to pay a tax to the Government for that service, and when the Government in turn regulates and pays those who provide it, that service is socialized and is subject to the evils of political control.

* * *

There is little evidence that compulsory health insurance will improve the health of the nation or that it is necessary to assure adequate medical care to the American people. There is much to suggest that such a program would gradually lower rather than continue to improve the quality of care received and that its cost would be inordinately high. We therefore oppose its adoption.

We believe that provision of adequate medical care for those unable to obtain it by voluntary prepayment plans or by direct payment is the responsibility of local or state government aided by charitable agencies and, if necessary, by federal grants-in-aid to state programs. Such a program is in no way dependent on compulsory health insurance.[16]

We recognize the necessity of spreading the cost of serious illness by the development of more effective voluntary plans than those available today. We believe that the medical care of those able to purchase it through such plans or by direct payment is the responsibility of the individual, not of the Government.[16]

The development and perfection of a complete medical care program presents many problems the solution of which is not yet at hand. However, the rapid advances in medical care during the past decade suggest that, given further opportunity and with the complete co-operation of all concerned, — the public, those furnishing the services and the various private and Government agencies, — this country can develop a most effective and efficient medical-care program and still retain the initiative and individual freedom that have made it so great.

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PRACTICAL ASPECTS OF BETTER MEDICAL CARE*

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BOSTON

IN A discussion of the plans for better medical service to the people of the United States it seems logical to me that we should take into account what has been accomplished along these lines. We can be justly proud of the fact that the American people have available to them better medical care than the people of any nation in the world. I wish to bring to your attention some of the important factors that have brought this about and to offer some feasible suggestions about how we may still improve this service to humanity.

MEDICAL EDUCATION

The basic principle of good medical care arises in the education of the physician. Thirty-five years ago anyone could choose the medical school that he found the cheapest or nearest to his home or on the basis of the reputation of some of its teachers. Through the efforts of the Council on Medical Education and Hospitals of the American Medical Association, standards were developed for the medical schools of this country. These standards were based on adequate equipment and a proper proportion of full-time teachers. About seventy medical schools in the country meet these requirements, and all but three or four of the ones that could not meet them have ceased to exist. Massachusetts was one of the last states to legislate against the substandard school, with the result that we have a large number of the graduates of such schools practicing in this state. Through the efforts of the graduate teaching program of the Massachusetts Medical Society and the introduction of the so-called Gallupe Plan, which urges hospitals to aid in the education of the physician, these men are becoming well trained, safe and valuable doctors in their communities. A survey is now being made in the eighteen medical districts of the Commonwealth to ascertain the effectiveness of this educational program with the view of expediting the situation as rapidly as possible.

HOSPITALS

Early in the history of the American College of Surgeons it became obvious that the educational background of the surgeon was the hospital in which he received his postgraduate training. On the basis of equipment, laboratories, nursing, records, staff conferences, pathological studies and so forth, standards were set up. A survey of all the hospitals of 100 beds or over in 1922 revealed that less than 13 per cent could fulfill these requirements for adequate patient care and adequate resources for the training of the surgeon. By constant effort on the part of the American College of Surgeons 94.6 per cent of these hospitals have now met the standards. If we include the smaller community hospitals down to 25-bed capacity the percentage drops to 90.

THE PUBLIC HEALTH SERVICE

Article II of the Constitution of the American Medical Association states: "The objects of the Association are to promote the science and art of medicine and the betterment of public health." The Public Health Service has always had the complete support of the medical profession. The prevention of disease is the first and most important concept of our entire medical care program. I am informed that there are many vacancies in the Public Health Service and that in many communities there are inadequate facilities. To correct these deficiencies we may accomplish our greatest improvement in the program for better medical care of our people.

Smallpox, typhoid fever, malaria, tetanus, scarlet fever and diphtheria took a heavy toll of our forebears. These diseases have been so completely reduced to a minimum that the average medical student may consider himself lucky if he has the opportunity to see a case.

RESEARCH

Through the elevation in standards of medical education and hospital facilities for research many life-saving contributions have been made. Diabetes and pernicious anemia are outstanding in this category. There are hundreds of well trained medical scientists working steadily to discover the cause of cancer, arthritis, multiple sclerosis, arteriosclerosis and many other diseases not yet conquered. The discovery and development of the sulfonamides, penicillin, streptomycin and other antibiotics has lowered the incidence of death from pneumonia, peritonitis, septicemia and other illnesses caused by bacteria to a remarkable level. The better understanding of the chemistry of the body and the methods of bringing about a chemical balance in the tissue fluids has contributed greatly to the safety of surgical procedures particularly. Through research we may hope to reduce the incidence of disease and thereby increase life expectancy.

SPECIAL AGENCIES

Here in Massachusetts we are particularly aware of the many voluntary agencies engaged in special

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fields to care for the victims of various diseases. Our Greater Boston Community Fund has about forty of these on their list for aid. In addition we are cognizant of the March of Dimes for poliomyelitis, the work of the Tuberculosis League, and the national campaigns for heart disease, diabetes and arthritis. The American people are so constituted that they not only recognize their obligation to their fellow men but also feel the satisfaction of service and the joy of giving.

Urban communities have naturally more nearly covered these problems than the rural districts have. It must not be overlooked, however, that such agencies as the Commonwealth Fund, with its direction toward hospital service and medical education, have demonstrated the possibilities along these lines. The Bingham Associates, in conjunction with Tufts College Medical School, have proved the value of their service to rural areas in New England.* The frontier nursing established by Mrs. Breckenridge in the mountains of Kentucky is familiar to most of us here in Boston. There are doubtless many other voluntary organizations functioning in various districts that are less well known to us.

The Present Situation

The results of our present efforts are well illustrated by the report of Dr. Louis I. Dublin,[1] Second vice-president and statistician of the Metropolitan Life Insurance Company, who states:

> . . . the American people never were healthier than in 1948, and the prospect is for continued improvement in 1949. The 1948 death rate will establish a new low in our country with a figure of slightly below 10 per 1000 population. This unprecedented record was achieved despite changes in our population structure, such as a large increase in the number of infants and a rise in the proportion of old people, both of which tend to increase the total death rate. Mortality rates in 1948 fell at every age period of life. The death rate from many important diseases touched new low levels, tuberculosis outstanding. In 1948 this disease will be down almost to 30 per 100,000, a reduction of about 40 per cent in the last ten years. The death rate from pneumonia was about 10 per cent under the previous low in 1947, owing largely to the ever-increasing use of sulfa drugs and penicillin. Infant and child health have achieved a splendid record, and mortality in infancy and childhood were at record-breaking low levels. Death of mothers in childbirth continued to decline. The mortality registered for chronic diseases of the heart, cancer and diabetes presented a different picture but show little change in the aggregate of the 1947 figure.

A further illustration is furnished by the following quotation:

> Out of 1000 live babies born, one-quarter, or 250 babies, were doomed to death before attaining age 24 under the mortality conditions of 1900–02. The comparable age is now 59, with the majority of surviving persons, of course, living a good many years longer. This improvement is nothing short of amazing. Think of it: Three-quarters of the rising generation, the vast bulk of our new citizens, have a minimum longevity expectation now nearly 2½ times greater than was the case a scant half century ago. And this statement does not allow for the further improvements which will be achieved, if present trends continue, during the lifetime of these new citizens.[2]

*The recently developed Nashoba health center in Townsend, Massachusetts, is an excellent illustration of the voluntary solution to the health problem. This unit, built in co-operation by five surrounding communities, is a matter of local pride, and may well be used as a standard pattern for areas throughout the United States.

The Problem

The indigent have for many years received good medical care. This is accomplished through various tax-supported measures at the local level and by various philanthropic agencies including the voluntary hospitals. It has been the part played in this type of care by the voluntary hospitals that has resulted in the almost insurmountable deficits with which these institutions are now struggling. With the high tax rates it becomes more difficult for public-minded and generous citizens to meet the needs. The cost of medical care has been more than doubled in the past few years. Wages of all hospital personnel except doctors have been increased, and the hours of work shortened. Although it may be proved statistically that a dollar today will buy what 50 cents would have bought before World War II, it certainly does not work out that way as far as hospital care of patients is concerned. One of the great needs at present is to arrange for some adequate source to cover the actual cost of the care of the indigent patient.

The well-to-do also get adequate medical care. They can afford the physician of their choice and pay the specialist or consultant a regular fee. They can also meet the increased costs of hospital and nursing care.

There is a large percentage of the population who earn enough for the needs of themselves and their families until a major illness intervenes. These people form the backbone of our industry and are the ones who must have a plan whereby they can feel independent and meet the crisis of illness without either resorting to charity, which they abhor, or running into bankruptcy.

A survey prepared for and released by the American Life Convention, American Mutual Alliance, Association of Casualty and Surety Companies, Bureau of Accident and Health Underwriters, Health and Accident Underwriters Conference, Life Insurance Association of America, Life Insurance Conference and the National Fraternal Congress of America shows that more than a third of the nation is protected by some form of voluntary hospital insurance. Voluntary insurance plans for surgical and medical expenses cover approximately 26,000,000 persons. Newer types of protection account for an estimated 9,000,000 persons. Under the benefits for loss of income due to disability, 31,000,000 persons are protected. This represents more than half the employed civilians in the country. The number of persons covered under group insurance policies and under Blue Cross plans is 56 per cent greater than that at the end of 1945 and 241 per cent greater than that at the end of 1941.

The carriers insuring against hospitalization expenses include insurance companies and fraternal societies, with an estimated 21,000,000 covered. Blue Cross Plans account for 28,000,000 persons.[3]

In Massachusetts these insurance plans cover 60 per cent of the population. Blue Cross alone protects 2,000,000 of the 4,500,000 people in this state. Blue Shield in Massachusetts covers 750,000 persons.

The rapid growth of these voluntary plans throughout the nation is evidence that a high percentage of our citizens are self-respecting, independent-minded people. It could well be estimated that these voluntary plans will within a few years take care of the majority. I think we should give this a more adequate trial since the growth of such measures has been so spectacular.

Under these plans Dr. Paul R. Hawley,[4] chief of the Blue Cross and Blue Shield Commission, says:

> . . . the quality of medical care now being furnished in the United States is highly satisfactory. The quantity of medical care available leaves something to be desired, especially in the matter of more hospital beds and more nurses in every community and more physicians in many rural areas. The cost of good medical care is a matter of concern to many people.

What Is Being Done

The Voorhees Subcommittee of the Hoover Commission has pointed out that there is a considerable amount of duplication and overlapping of effort in the Government-controlled medical services. It is heartening to learn that cognizance of this study is already taking effect. Early in January, 1949, the following information was released:

> Secretary of Defense Forrestal made public the most detailed list of recommendations yet submitted by the Hawley Board, coincident with the first meeting of the new civilian advisory group which will succeed that board. The report, which Forrestal emphasized, has not yet received his approval, calls for decommissioning of two Army and one Navy general hospital; reductions of three Army general hospitals to station status and of 48 Army station hospitals to dispensaries; joint staffing of military medical installations that are used in common by personnel of Army, Navy and Air Force; joint utilization of specialists and consultants; establishment and joint staffing of specialty centers — tuberculosis and neuropsychiatry, for example. Signers of the 75-page report were Dr. Paul R. Hawley, chairman; Surgeons General Raymond W. Bliss (Army) and Clifford A. Swanson (Navy); Air Surgeon Malcolm C. Grow and Rear Adm. Joel T. Boone, executive secretary of the board.[5]

We now have more doctors per capita (1:710) than any nation in the world except Jewish Palestine, which is admittedly a temporary situation. It is true that the doctors are not evenly distributed, and there tends to be concentration in cities and in states regarded as having more pleasant climatic conditions. We may find that arrangements can be made to obtain a better distribution and therefore better service to those areas that need it. The statement so often made that we need more doctors requires further study. Perhaps we do, and if so something will be done about it.

That we do have a shortage of nurses seems apparent to all. When we take into consideration that the first graduate nurse, Linda Richards, received her diploma from the New England Hospital for Women and Children in Boston only seventy-five years ago it really seems miraculous that we are as well off as we are. Efforts are being made and plans are in operation to supplement the trained nurse with one of less training to carry much of the load. This major problem in the care of the sick will, I am sure, adjust itself into a much more rational and logical plan of nursing care than we have had in the past.

We have been agreeably impressed with the functioning of the Veterans Administration. Under the guidance of Dr. Hawley and Dr. Magnuson the American veterans receive better medical care than any other group of people. This was brought about by the selection of the staff doctors of Veterans Administration hospitals by so-called dean's committees. Full-time heads of services are well trained men. To help them, there are as many part-time consultants as are needed. These men are from the teaching institutions and bring all the new, tried and tested products of the research laboratories and medical clinics of the community to the veteran. There is no opportunity under such a system to subject these patients to obsolete methods or political rackets.

It is necessary for us to explore completely the medical needs of the nation. Each state must make its own survey. What is lacking in Massachusetts will probably be quite different from the shortcomings in Mississippi. Having done this in a careful manner, we should find ways and means of correcting the deficiencies.

On the basis of the experience of the Veterans Administration, I believe that a health plan for the nation could be evolved that would completely take care of the situation. This must vary according to the needs of the locale. Perhaps the most important problem is public health in a broad sense. This may be interpreted as including diagnostic facilities. In many places the facilities are already available, including existing hospitals both voluntary and Government controlled. In many areas the Veterans Administration hospitals already existing and those in the process of construction could serve. In some areas special diagnostic centers will need to be built. It would be possible in isolated areas for special diagnostic features to utilize mobile units.

These diagnostic centers should be under local and state control and the staff approved by the medical schools or, in states where no medical school exists, by the universities. It should be made possible for any citizen to avail himself of this diagnostic clinic. It he can afford to pay he should do so. If he has hospital insurance this should be taken into account. If he is indigent his services

should be paid for on a prearranged schedule by the community — a part by the local taxpayers,[4] a part by the state and a part by philanthropy, the deficit under such a plan being borne by federal taxation.

This, some of us think, would work, and it would assure the best medical service available in the country and would not be hampered by politics. It would cost something, but it would cost a great deal less than any federal-controlled, compulsory scheme that has been suggested, and it would not interfere with the system of free enterprise on which this nation was founded and on which it has grown to be the greatest nation in the world.

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MEDICAL PROGRESS

PSYCHOSURGERY

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BOSTON

AN EDITORIAL[1] in 1940 referred to "radically wrong," "meddlesome surgery," which was a "violation of the Hippocratic oath." An opposing view was expressed by Fiamberti[2]: "In the present state of affairs, if some are critical about lack of caution in therapy, it is on the other hand deplorable and inexcusable to remain apathetic, with folded hands, content with learned lucubrations upon symptomatologic minutiae or upon psychopathic curiosities, or, even worse, not even doing that." The first opinion is written by a man who fears an indiscriminate cutting of lobes and hemispheres by unconscionable surgeons, and the second by one who is motivated by the depressing picture of the hopeless, deteriorated, backward schizophrenic patient. Strong opinion and emotional bias continue to becloud the issue of psychosurgery.

The earliest psychosurgery is accredited to G. Burckhardt, superintendent of a mental hospital in Switzerland, who, in 1890, operated upon the brains of 6 disturbed psychotic patients. There was 1 postoperative death, 1 recovery and at least 2 postoperative convulsive complications. But Burckhardt was impressed with the possibilities of this method.

At the International Neurological Congress held in London in 1935, Fulton and Jacobsen[3] reported briefly on behavioral changes that developed in 2 chimpanzees after bilateral ablation of the frontal association areas. Stimulated by this report, Egas Moniz,[3, 4] in 1936, introduced bilateral prefrontal lobotomy in man.

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Types of Procedures

Bilateral Lobotomy (Leukotomy)

Moniz and the neurosurgeon Lima first tried injection of alcohol into the frontal association areas and later invented a leukotome, a trocar-like instrument from the end of which a wire loop or a cutting edge could be protruded. Rotation of this loop within the frontal lobes cut cores in the white matter. Moniz made a superior approach on either side, 3.0 cm. from the midline, and 1.5 cm. anterior to a vertical line passing through the base of the tragus. He advised cutting four to six cores in each frontal lobe located at various subcortical levels. Among the complications encountered were sphincter disturbances, sluggish pupils and anisocoria. He also called attention to transient apathy, loss of initiative and disorientation, and said that there were "no grave repercussions in the part of intelligence or memory." Moniz stated that a third of his patients recovered, a third improved, and a third were not benefited. His best results were in agitated depressions, and his poorest results were in chronic schizophrenia.[4]

The Moniz technic has been modified, wholly or in part, by many surgeons. In America, the first lobotomies for mental disease were done in 1936 by Freeman and Watts, who became the chief proponents of psychosurgery in this part of the world. Their experiences with over 500 lobotomy cases have been summarized in a series of publications,[5-28] including a scholarly and interesting book, based on the first 80 cases, written in 1942.[29]

Freeman and Watts have used a lateral or temporal approach entering at a point 3 cm. behind the outer canthus and 6 cm. above the zygoma. A blunt knife is introduced, with proper precautions

against too deep an entry, and the white matter in each frontal lobe is then severed along the coronal plane. Freeman and Watts have emphasized careful localization of the point of entry and adjustment of the plane of section in relation to clinical requirements. Deviation of the plane of section by as little as 5 mm. may spell the difference between success and failure.[22] Their standard operation has been used in 63 per cent of their cases, a radical or more posteriorly placed section in 37 per cent, and two or more operations in 12 per cent.[9, 26] More anteriorly placed sections are employed in affective disorders, and more posteriorly placed sections in the schizophrenic disorders. Reoperations are usually done in a more posterior plane. The more anterior the incision, the less alteration in the patient's behavior, and the more posterior the incision, the greater the likelihood of interfering with area 6, with subsequent prolonged incontinence, convulsive seizures or transitory Babinski and grasping reflexes.[15] Although the location of the plane of section is doubtless important, Mettler and Rowland,[30] on the basis of post-mortem studies, have pointed out that even when the Freeman and Watts lobotomy point is carefully defined on the skull, there is significant variation in the location at which the leukotome is inserted into the brain.

Yahn[31, 32] has recently reported on 209 cases, 161 of which were operated on by the Moniz method and 48 by the Freeman and Watts method, but unfortunately for this comparison many of the latter were previously operated on by the Moniz technic. Yahn believed that superior results were not necessarily to be expected from the more extensive cutting in the Freeman and Watts technic. Although his results are not conclusive, the work represents one of the few attempts to compare different procedures in a single clinic.

Another noteworthy modification of the psychosurgical procedures has been developed by McGregor and Crumbie[33] in England, where there is considerable enthusiasm for the surgical treatment of serious mental disorders.[34] McGregor and Crumbie have devised an instrument with a rotating blade that is introduced 3 cm. behind the eye and 5 cm. above the zygoma and cuts a core 3 cm. in diameter in the center of the lobe, in the coronal plane. The Great Britain Board of Control,[34] which in 1947 reviewed 1000 cases submitted to psychosurgery in various English centers, stated that there was little uniformity in the neurosurgical method used in that country.

Ström-Olsen and his associates,[35] in 1943, used both the Crumbie technic and the method of Freeman and Watts, separately and combined, in 30 chronic cases with no hope of recovery by other methods and arrived at the conclusion that the Freeman–Watts procedure should be used in long-standing psychotic conditions, and the Crumbie technic in the less severe cases.

In June, 1937, Lyerly[36] did the first "open" operation. Approaching each frontal lobe superiorly, he turned a rectangular osteoplastic flap and with the aid of a specially lighted speculum attempted to separate the white fibers under direct vision. Lyerly took pains to separate particularly the inferior frontal fibers because they connect frontal lobes with thalamus and hypothalamus — areas that are believed to have an exceptional role in the regulation of emotion and states of tension. Perhaps the chief exponent of the Lyerly technic is J. L. Poppen, who with his associates has performed over 500 lobotomies by this method since 1943. Poppen[37] has introduced minor modifications of his own but adheres to the principles of superior approach, direct visualization of everything that is done and strict attention to fibers in the inferior or orbital aspects of the frontal lobes. The proponents of the "open" method believe that hemorrhage can be more successfully avoided by this technic, that it is possible to localize more accurately the plane of section in relation to cerebral structures, and to estimate more reliably the percentage of white fibers cut in that plane.[37, 38] Statistics presented before the International Conference in Psychosurgery in 1948[39] indicate that the mortality is higher in the "closed" than in the "open" method. A recent poll of neurosurgeons in this country[40] reveals a preference here for the open technic; in foreign centers "closed" methods still prevail. No superiority for either procedure has been claimed in relation to postoperative seizures.

Unilateral Lobotomy

At a panel discussion in 1941, Lyerly[41] reported that he had done unilateral lobotomies in 4 cases, with good psychiatric results. The change was not so striking as when the operation was done on both sides, but a good unilateral operation might be as good as a partial bilateral operation. Freeman and Watts,[29] however, on the basis of their experience, concluded that both lobes must be operated on to obtain good results. Gayle and Neale[42] and Van Waganen[43] also had unsatisfactory results with unilateral lobotomy.

On the other hand, there are data to suggest that unilateral lobotomy cannot be considered therapeutically worthless. Schwarz[44] performed a therapeutically successful unilateral lobotomy in a patient with a long history of a depressive state that showed a potentiality to remit after electroconvulsive treatment. Meyer and Beck[45] noted a case that showed considerable clinical improvement after a unilateral leukotomy.

Scarff[46] reported 10 cases in which ipsilateral, contralateral or bilateral pain was treated by unilateral lobotomy. The results were good in 7 cases. There was suggestive evidence that pain was more successfully relieved if the ipsilateral dominant

lobe were cut than if the contralateral nondominant lobe were cut. Curiously, 2 patients with bilateral pain were relieved by a one-sided operation. The results of the Boston Psychopathic Hospital group[47, 48] on unilateral lobotomy certainly indicate that further study of this operation for mental disturbances or for chronic pain would be eminently worth while.

Bilateral Orbital Leukotomy

Much thoughtful consideration has been given to avoiding unnecessary sacrifice of brain tissue. Some workers have been particularly impressed with an array of observations that have pointed up the special significance of the inferior or orbital aspects of the frontal lobes in determination of the personality. When Freeman[49] first experimented with the coring method of Moniz, he observed that "cores in the lower part of the frontal lobes produced a higher incidence of good results than cores placed in the upper part of each frontal lobe." Dax and Radley Smith,[50-52] using the McGregor–Crumbie leukotome and with a temporally oriented approach, carried out important studies of the comparative effects of leukotomies in various parts of the frontal lobes on separate series of cases. In 1946 they reported the results in patients who had received an "upper section," a "middle section," and a "lower section."[51] In some cases horizontal sections were also made. These authors reported that depressions were most readily relieved by lower sections, aggressiveness of catatonic schizophrenia by an upper incision, and paranoid schizophrenia by a middle and horizontal section. In 1948 before the International Conference of Psychosurgery,[52] they spoke of the desirability of the use of inferior or orbital sections in passive, apathetic depressions, in which the operation releases hyperactivity, euphoria and extroversion, and of superior or high sections, cutting fibers from areas 9 and 10, in cases with increased psychomotor activity. Additional middle and horizontal sections were used when more extensive leukotomy was desired.

In 1945, Hofstatter, Smolik and Busch[53] reported on 30 cases in which they had sectioned only the inferior quadrants bilaterally, using the Freeman and Watts method. They described improvement in 3 cases with affective psychosis, 1 with obsessive-compulsive neurosis, a decrease in somatic complaints in neurasthenia and significant improvement in various types of schizophrenia.

In two recent reports, Reitman[54, 55] further analyzed the cases operated upon by Radley Smith and stressed that the postoperative adjustment of patients who had received the orbital cut was superior to those with sections located elsewhere. Concerning the orbital cut, patients showing shallow affect, introversion, depersonalization or lack of initiative responded better than those suffering tension, anxiety, restlessness or aggression. Symptoms such as euphoria, overactivity and extroversion (often coupled with aggressiveness) were most likely to follow the orbital leukotomy.

Frontal Lobectomy (Unilateral and Bilateral)

Frontal lobectomy, prior to the advent of psychosurgery, was done only for serious disease in the frontal areas — tumors, epileptogenic scars, chronic abscess, meningocerebral adhesions or brain-crushing injuries of the frontal lobes. Prefrontal lobectomy has been extended by Peyton, Noran and Miller[56] to the treatment of mental illness in the absence of gross intracranial disease. This method was chosen because it allowed direct visualization of the operative field, the plane of section could be determined by visible landmarks, and the field could be inspected against hematoma. Furthermore, cerebral tissue could be removed, weighed and examined microscopically, and no devitalized tissue was left behind. Fourteen cases were reported in February, 1948, including 3 of severe psychoneurosis and 11 of schizophrenia — all with hopeless prognosis and five years or more of hospitalization. One patient died of accidental ligation of the anterior cerebral artery. Sensorial clearing required ten days on the average. Convulsive seizures developed in 4 cases. No patient made a complete recovery; 2 were considered markedly improved, and 9 moderately improved. Psychometric tests were not quoted.

Transorbital Lobotomy (Bilateral)

Fiamberti[2] (1937) thrust a "trocar" through the orbital plate and then either injected 10 per cent formalin or cut cores in the white matter of the frontal lobes with the Moniz leukotome. Freeman[28] determined on cadavers that by this method openings in the orbital plate could be made well behind the frontal sinuses, lateral to the ethmoids and anterior to the attachment of ocular muscles. Openings into the base of the frontal lobes were 3 cm. lateral to the longitudinal fissure and 2 cm. behind the frontal pole. Fibers in the central portion of the frontal pole were severed anterior to the rostrum and insula. The anesthesia was achieved by two or three electric shocks.

Postoperatively, Freeman[28, 57] stated that the patients had little more disturbance than would be attributable to the electric shocks. Fatuous euphoria, bland indifference and purposeless activity, often seen after the standard lobotomy, were not observed, but striking relief from anxiety was experienced by the patients, as with the conventional lobotomy. Complications were observed in only 2 of 10 cases, and incontinence was seldom seen. A third of the schizophrenic patients and half the involutional patients responded favorably to operation combined with electric shock. None of the unfavorable personality defects noted after prefrontal lobotomy were observed after transorbital

lobotomy; therefore, Freeman has suggested considering this operation earlier in the course of serious mental disease.

Jones and Shanklin[58] used the transorbital lobotomy in 41 chronic cases. Worthwhile results (good or fair) were obtained in 80 per cent of the group. There was marked relief of anxiety and inner turmoil. The patients were ambulatory shortly after the anesthesia had worn off. The only significant complications were orbital ecchymosis, enuresis (in 3 cases) and transient unilateral ptosis (in 1 case). The authors recommended transorbital lobotomy in patients refractory to electric-shock treatment, for whom a major lobotomy was contraindicated.

Topectomy (Bilateral)

In March, 1948, the Columbia–Greystone Associates[59] announced that a study was in progress to determine the effects of bilateral removal of areas of frontal cortex upon chronic mental disease. This study was undertaken in an effort to treat patients by means of a relatively small and precise surgical lesion, and to avoid the undesirable personality defects that often accompanied conventional lobotomy. An attempt was made to control the study by simultaneous observation of matched cases in which the patients received sodium amytal and phlebotomy.[60] An open-bone-flap operative procedure was utilized, and the areas removed included in all cases the medial or parasagittal portion of the superior frontal gyrus, approximately the rostral third of the superior frontal gyrus and an adjacent portion of the middle frontal gyrus. In patients studied less than a year, Lewis[61] reported almost specific reduction in psychotic anxiety, no impairment in intelligence, learning, memory or abstraction, and no deaths, convulsions, persisting incontinence or personality deficits. The percentage of paroles after four months among patients operated on was significantly higher than that among controls. Removal of Broca's area did not lead to aphasia, and removal of the premotor area resulted in no permanent loss of motor function. LeBeau[62] has done topectomies in 10 cases of uncontrollable agitation. There were 3 postencephalitic cases, 2 manic-depressive cases, and 5 patients suffering from epileptic seizures. LeBeau observed no blunting of the personality or social initiative and no change in convulsive episodes. No deaths occurred in the group. He also removed areas 9, 10 and 46 bilaterally in 8 cases of intractable pain, with therapeutic benefit. LeBeau considers the results of bilateral topectomy as good as those of lobotomy, although the former operation is a major surgical procedure.

Thalamotomy (Bilateral)

A psychosurgical technic that has received considerable lay and professional attention is thalamotomy, introduced by Spiegel et al.[63-65] By stereotoxic methods they made small circumscribed lesions in subcortical areas, with only minimal injury to overlying cerebral structures. In the treatment of psychoses, it was necessary to make at least five lesions in each dorsomedial thalamic nucleus with destruction of approximately a seventh of the nucleus before appreciable results could be obtained. Eight patients were operated upon, with 1 death, and 4 were sufficiently improved to go home. The method can be used in the treatment of unbearable pain by combining lesions of the spinothalamic system in the midbrain with lesions of the dorsomedial nucleus of the thalamus (mesencephalothalamotomy). The procedure was also recommended for treatment of convulsive disorder of subcortical origin.

Cortical Undercutting (Bilateral)

This method was recommended by Scoville[66] as a substitute for psychosurgery of the ablation type, which generally requires several tedious hours and large cranioplastic bone flaps. Scoville's operation is done in one hour, requires two trephine openings and produces little bleeding. The areas selected have been areas 9 and 10 of Brodmann (because of the success reported by others in ablation or leukotomy of these areas) and the orbital and cingulate areas because of their known influence on the autonomic nervous system and personality of animals. Undercutting of the posterior orbital surface (areas 13 and 47 of Brodmann) has not produced the sham rage and maniacal behavior reported in animal ablations of these areas.

The psychiatric and therapeutic results of this operation are not as yet available.

Bilateral Medial Lobotomy (Bimedial Lobotomy)

In 1945 Smith[67] showed that the anterior cingulate gyrus when stimulated produced autonomic effects — dilatation of the pupils, piloerection and cardiovascular and respiratory changes. Smith ablated the anterior cingulate gyrus (area 24) in monkeys and observed they became unusually tame and easy to handle, and Ward[68] noted that the animals lost shyness, fear of man, hostility and "social conscience." Ward suggested that psychotic patients might be benefited by an operation restricted to the cingulate area, a more radical lobotomy being thus avoided.

These considerations among others prompted workers at the Boston Psychopathic Hospital[69] to observe a series of cases in which the medial aspects of both prefrontal lobes were sectioned in an "open operation," using the superior approach of Lyerly and Poppen. Particular effort was directed toward sectioning of the white matter related to the anterior cingulate gyrus on either side. Thus far the results in 14 cases followed four to six months indicate that the bimedial operation is therapeutically efficacious. Five patients were significantly

improved, 4 of whom were discharged home. Many symptoms characteristic of patients who received a full bilateral lobotomy were also found in patients who received bimedial or unilateral lobotomy — for example, weight gain, increased appetite, outspokenness and reduction in activity level.

Anatomic Considerations

The great variability of lesions produced by psychosurgery has been stressed by Dax et al.,[51, 52] Meyer, Beck and McLardy[70, 71] and Yakovlev.[72] The plane of insertion of the leukotome and also the amount of hemorrhage varied considerably in the cases reported by Meyer and his co-workers. In some of their patients who recovered the lesions were surprisingly incomplete and circumscribed, and structures near the midline were not involved. In other cases, either considerable improvement followed unilateral leukotomy, or the damage to one frontal region was negligible. In one case the prefrontal lobes were not involved at all.

McLardy and Meyer[71] indicate from pathological correlations with clinical improvement that no coronal segment is always involved when improvement occurs, although the central segment comes closest to being so. More segments were involved in the improved than in the unimproved group, and greater improvement, as a rule, occurred with the more posterior cuts.

Freeman[29] calls attention to degeneration of the medial dorsal nucleus of the thalamus as one of the constant findings in pathological specimens. Projections from the thalamus to the cortex are apparently much stronger than those from the cortex to the thalamus. Damage to the anteromedial nucleus and to the lateral ventral nucleus may also occur.

The pathological studies yielded new data concerning anatomy of the thalamus. They established the fact that in man the central part of the medial dorsal nucleus projects upon the frontal pole, the medial portion on the base, and the lateral portion upon the convexity. Freeman believes that the pathological studies lend support to the hypothesis that the medial dorsal nucleus is the anatomic substrate for emotional experience.

Tracts theoretically divided by a full bilateral prefrontal lobotomy are those connecting the thalamus with the frontal cortex, the prefrontopontine system or Arnold's bundle, the corticostriate tracts, the uncinate fasciculus, the fasciculus cinguli and the long association tracts.

LeGros Clark[73] cautions against assuming that the frontal cortex is merely an association area, for the frontal cortex is also an important afferent projection area similar to the visual or auditory cortex. He stresses the intimate two-way connection between the frontal lobes and hypothalamus. The dorsomedial nucleus is essentially a relay station for transmission of impulses originating in the hypothalamus to the frontal lobes, and the anterior nucleus of the thalamus, which projects upon areas 23 and 24, is the terminal station of the mammillary body that receives the afferent tracts from the whole of the hippocampus (fornix system). Areas 23 and 24 (anterior cingulate gyrus) are now thought to have suppressor functions like areas 8, 6 and 4.

Thus, a great portion of the frontal-lobe cortex may be regarded as a projection area, receiving the products of activity of the hypothalamus in the same way that the visual cortex is the projection area for retinal activities.

Theoretical Considerations

In developing the concept of the use of surgery in the treatment of mental disease, Moniz believed that in the abnormal personality, pathologic ideas dominated the patient's mind, becoming fixed by the functional grouping of certain cells in abnormal relations in the frontal areas, and that beneficial results could be wrought only by destroying these morbid constellations.

Freeman, at first, was impressed by the marked reduction of tension in lobotomized patients and particularly the diminution of affect that formerly attached to pathologic ideas. This in turn seemed to be the very basis of the new interest in the outside world and appeared to release energies formerly trapped within the morbid framework. The thalamus was seen as an important emotional center that provided the energy connected with pathologic ideas, and severance of connections between thalamus and frontal cortex was the necessary step to reduce the emotional charge of abnormal ideas or to "bleach" the affect attached to those ideas. According to Freeman, the patient is fundamentally overly concerned with himself, suffers from anxiety and tension as he sees himself in relation to other human beings and to society at large; after the operation self-consciousness is reduced, foresight and insight are diminished, and emotion, which is still present, attaches itself to external happenings rather than to inner experience. Thus, after lobotomy the hallucinated patient may still hear voices but is not bothered by them, and the patient with cancer and fear of death casually admits to pain but is no longer deeply concerned.

Recently, Freeman has stated that foresight and insight are no longer tenable as hypotheses to explain the function of the prefrontal lobes and has focused his emphasis upon consciousness of self in its manifold forms as the primary business of the frontal lobes.

A further hypothesis that has been advanced tries to relate the function of the frontal lobe to the structure of modern dynamic psychology. According to this theory, damage to the prefrontal areas impairs the patient's "ability to perceive *threats* to his ego-organization." Since his formerly

marked defensive reactions are no longer called into action, he is freed from maladaptive behavior.

Indications and Results

Lobotomy has generally been considered a procedure of last resort.[23] Consequently, the patients, particularly in the early stages of its use, represented hopeless and chronic forms of mental disease, for the most part relegated to custodial care. Some of them were particularly disturbed persons who, because of hyperkinetic syndromes and suicidal or homicidal impulses, were troublesome problems of management to hospital administrators.[74, 75] The follow-up studies of this material have helped to sharpen the indications somewhat, but large clinics have not departed from the use of the operation as a last resort, doubtless because irreversible brain destruction is implicit in this form of treatment.

Freeman and Watts[24] offer the opinion that results of prefrontal lobotomy are slightly better in females, Jews and Negroes. Better results have been reported for mental disease of short duration than for disease of long duration, but, especially in the affective disorders (manic-depressive and involutional psychosis), duration of illness is not so important as clinical picture, degree of tension and so forth. Patients with higher education are likely to make better postoperative adjustments than those with meager educational possibilities.

From the point of view of nosology, lobotomy is first indicated in the affective psychoses (involutional psychosis and manic-depressive psychosis) that have been disabling for long periods and refractory to electric-shock treatment. In manic-depressive psychosis when more than half the patient's lifetime is spent in the hospital, lobotomy should be seriously considered.[76, 77] The results in the affective disorders have been encouraging, and many who would otherwise have been doomed to untold months of misery have been relieved of their suffering and reclaimed to some degree of useful living.

Data gathered by Walker[78] from 12 authors indicated that of 150 patients with affective disorders treated by psychosurgery 63 per cent made social recoveries, 19 per cent were markedly improved, 13 per cent showed little or no change, and 3 per cent died. In 250 cases classified as manic-depressive collected by the Great Britain Board of Control,[34] 48 per cent of patients were considered recovered and 35 per cent improved. Considering the lack of uniformity in surgical procedures and in methods of appraising results, the similarity of results from various centers is astonishing.[12, 16, 17, 42, 79-86] Satisfactory outcome is uniformly reported in a half to three fourths or more of the cases.[12, 16, 17, 42, 79-94]

Lobotomy has not been so successful in schizophrenia as in the conditions mentioned above. Insulin and convulsive-shock therapy are considered therapeutic prerequisites in schizophrenic patients prior to lobotomy provided that a significant possibility of improvement with these therapies exists.[75] Patients with paranoid and catatonic schizophrenia usually fare better than those with simple or hebephrenic types. The familiar factors that are recognized as favoring a more hopeful outcome — such as good prepsychotic personality adjustment,[95] sudden onset, a clinical picture featuring turmoil[74, 96] and depression,[94] remitting tendency and favorable, if temporary, response to convulsive therapy — also apply in shaping the prognosis of schizophrenic patients after lobotomy.

Walker[78] collected information from 16 clinics indicating that of 298 schizophrenic patients who received lobotomy 17 per cent made social recoveries, 24 per cent were markedly improved, 59 per cent showed little or no change, and 0.7 per cent died. The results collected by the Great Britain Board of Control[34] revealed that of 599 patients 16 per cent recovered and 63 per cent improved. In most series, about a third of the cases of schizophrenia show good results.[15, 17, 31, 32, 51, 52, 54, 74, 75, 89, 90, 97-115] Only Heilbrunn and Hletko[116] were disappointed with their results in 11 adult patients with schizophrenia, and Freeman and Watts[21] with their results in 11 cases of schizophrenia that had begun early in childhood.

Considerable enthusiasm exists for the use of lobotomy in long-standing obsessive-tension-ruminative states that have been progressively disabling.[9, 11, 17, 74, 91, 93, 97, 117, 118] Of 29 patients with psychoneuroses primarily of this type studied by the Great Britain Board of Control[34] 7 per cent recovered and 59 per cent improved.

Thorpe[119] and Rizzatti[120] pointed out the value of lobotomy in severe behavior disorders associated with psychoses of chronic encephalitis.

Lobotomy has been considered contraindicated for constitutional psychopathy associated with cruelty, aggression, irresponsibility[24] and antisocial habits.[121-123] Alcoholism is not improved by lobotomy and may be made worse.[29] Organic deterioration from severe arteriosclerosis, senility, general paresis and so forth has been considered a contraindication by some authors (Frank[124]). Myerson and Myerson[88] have reported good results in chronic depressive states in patients over sixty years of age, and point out that age in itself does not necessarily contraindicate lobotomy provided the clinical picture is a favorable one.

Freeman and Watts [18, 19] noted that some patients who suffered from severe pain coupled with anxiety, depression, gloomy foreboding and fear of death were greatly relieved after lobotomy. When the fear of future disability was allayed, pain was borne with equanimity. The operation has been applied in pain of phantom limb, focal neuralgia, mucous colitis, crippling arthritis, anginoid syn-

dromes, tabes, carcinoma,[25] and so forth. Poppen[38] described the case of a hopeless drug addict who was bed ridden, emaciated, and in constant torture because of severe discomfort and pain in the left side of the head along the distribution of the fifth nerve — although it had been divided intracranially. After lobotomy this patient was marvelously improved, and no longer required morphine. Hawkes and Gotten[125] compared prefrontal lobotomy with cordotomy for relief of intractable pain associated with carcinoma. Cordotomy was followed by extreme weakness, bladder paralysis and often incomplete relief of pain. Lobotomy produced spectacular relief of pain and nullification of anxiety relative to the carcinoma, and, furthermore, no narcotics were required after lobotomy. Lobotomy was considered far superior to cordotomy in the relief of intractable pain.

Scarff[46] has recently tried unilateral lobotomy for relief of pain with notable success. Dynes[48, 126] reported on both bilateral lobotomy and unilateral lobotomy in a series of cases of pain studied at the Lahey Clinic. Relief of suffering was accomplished by this operation. In general, patients with metastatic cancer were more greatly benefited than those who displayed an exaggerated pain response in the presence of long-standing emotional instability. No anxiety, fear or concern over impending death was manifested in cases of cancer. The results appear to establish this procedure as a definitely useful tool in selected cases in the fight against unbearable pain.

Several authors have stressed symptom traits or syndromes that correlate well with eventual outcome. For example, a good deal of emotional tension ("tortured self-concern") is considered a favorable sign. Excitement, resistiveness, stupor, destructiveness and combativeness are favorable in schizophrenia, whereas docility, vagueness and apathy are contraindications.[15] Peters[127] analyzed statistically a large number of preoperative traits and came to the conclusion that a heightened activity level (restlessness, agitation, euphoria, excitement and so forth) was favorable to improved social adjustment after lobotomy. Particularly beneficial results have been claimed for excited psychotic patients with pulmonary tuberculosis; lobotomy apparently provides much needed physical and mental rest.

Taxing clinical judgment is the decision not only whom to lobotomize, but *when* to lobotomize. The operative risk, possible personality deficits and the disadvantages of delay must be weighed against the probabilities of obtaining comfort, more satisfactory social and economic adjustment and a place in the community.

Postoperative Confusion

Freeman and Watts believe that patients showing the best postoperative results are those who are confused, dull and retarded for several days or weeks after the operation. Confusion following sectioning of the fourth and last quadrant is taken as a sign that a sufficient number of white fibers have been sectioned. Kisker,[128] Meyer[70] and Petersen,[98] however, have not found confusion to be a significant element in improvement, whereas Gayle and Fishburn[97] believe that there is a somewhat better outcome in cases with postoperative confusion and incontinence.

Complications of Lobotomy

Among the physical and neurologic complications of prefrontal lobotomy, Freeman and Watts[29] list vomiting, sweating, blood-pressure change, borborygmus, coma, ocular changes, frontal ataxia, staggering, fainting spells, heart changes, intolerance to drugs and hemichorea — as symptoms that do not persist. Symptoms that may persist include increased appetite, masked facies, vesical incontinence, rectal incontinence, convulsions, Babinski sign, aphasia, reflex grasping and hemiplegia. Sphincter disturbances have been mentioned by Ström–Olsen[35] and Peyton et al.[56]

Convulsive seizures, a significant operative complication, have been reported from many centers. Stevens and Mosovich[109] reported an incidence of 33 per cent among 30 cases. Peyton et al.,[56] using bilateral frontal lobectomy, reported 4 cases among 14 patients operated upon, and Watts and Freeman[26] an incidence of 12 per cent among 250 cases. At the Boston Psychopathic Hospital the incidence of postoperative seizure complication has been about 10 per cent in 500 cases.[129] The seizures are usually few in number; however, many seizures and status epilepticus have been observed. The onset varies between days and years after operation; the larger number develop seizures between three months and one year postoperatively.

Grand mal is the principal type of seizure recorded by Greenblatt and Levin[130]; Jacksonian seizures and attacks of rigidity were observed in a few cases only. No petit mal or psychomotor attacks were noted.

Deaths

The reported mortality has ranged from 1 to 4 per cent in the larger series — somewhat higher in "closed" than in "open" operations. Cerebral hemorrhage is the prime cause of death, with meningitis, pneumonia, ligation of the anterior cerebral artery, cardiac failure and anesthetic sensitivity claiming occasional lives.

Deterioration

Perhaps because of the hopeless nature of most cases in which the operation was performed, patients considered worse after lobotomy were indeed rare. Eleven cases were mentioned out of 1000 collected by the Great Britain Board of Control[24] and 8 out of 618 collected by Zeigler.[131] Other au-

thors have casually mentioned that such cases are rare, without discussing them in detail.

Relapse Following Improvement

Four cases of relapse are mentioned by Dax and Radley Smith[81] among 129 patients who received operation, 8 of 100 by Parker[93] and 4 of 200 by Frank.[92] Details are inadequate.

Studies

Psychologic Studies

Hunt[132] was the first to study cases of prefrontal lobotomy. Forty selected patients operated on by Freeman and Watts were observed before and three weeks or longer after operation, a large battery of tests being used. Hunt found no evidence that total intelligence was decreased. Speed of performance was slowed, but accuracy improved on the average. There were better attention, fewer peculiar responses and greater tendency toward objectivity. Some patients accomplished more work with less strain and fatigue.

Kisker[133-136] studied Rorschach tests in 20 cases followed up to one year after lobotomy and found that the differences before and after lobotomy were not substantial. Improvement in performance of the Rorschach test and clinical improvement did not necessarily parallel each other. "Organic" signs were usually attributable to the psychotic process, and in general it was difficult to separate the psychotic, preoperative personality from the effects of the lobotomy.

Robinson[137] studied 10 selected cases in which the patients received lobotomy against 10 control cases matched for diagnosis and Binet vocabulary score. Many tests were pressed into service, some aimed specifically at suspected deficit areas. Again no impairment in general intelligence appeared.

Porteus and his colleagues[138-140] found insignificant changes in I. Q. tests (Binet) but marked impairment in the maze test. The maze test is purported to measure planned initiative, foresight, executive ability, capacity to consider several possibilities at once while action is delayed and power to sustain attention.

Babcock[141] carefully studied a case of anxiety neurosis before and after lobotomy, and her results were interesting because her subject lacked the gross psychotic personality disintegration of most of the other patients studied psychometrically. The patient was quicker after lobotomy but made more errors, had a shorter memory span, could not recall as much of what he learned, was slower at perception of new conditions and demonstrated poorer judgment.

Other psychometrists such as Van Waters,[142] Brody[143] and Atwell,[144] agree that although personality changes may be grossly apparent, evidence of brain damage due to the lobotomy is not regularly observed, that many of the supposed postoperative defects in performance may be related primarily to changes in attitude, and that there is often a tendency in the favorable case to recuperate from functional losses.

Halstead's[145-147] work is significant from the standpoint of failure to demonstrate brain damage in lobotomy cases by tests that proved highly differentiating in head injury, lobectomy and anoxia.

Malmo[148, 149] reports an outstanding exception to the generally negative results of other writers who used I. Q. tests. In 7 cases of bilateral frontal gyrectomy and 8 of bilateral frontal lobotomy, he found a consistent drop in general intelligence as measured by the Bellevue–Wechsler intelligence scale.

In general, it may be said that the psychologists have reaped a poor harvest so far as tests of general intelligence or brain damage are concerned. The many strikingly negative results in cases with gross frontal lobe destruction have pointed up the coarseness of the present psychologic instruments used for detecting brain damage. These studies have also demonstrated that lobotomy produces much less disruption of psychologic function than lobectomy does.

Psychologic tests for personality changes have been more fruitful, on the whole, but as yet have brought forth little of definitive value in the realm of measurements of drive, of frustrational response or of social dynamics.

Physiologic Changes after Lobotomy

During the operation, cold clammy extremities often become warm and moist, the blood pressure falls particularly after sectioning of the last quadrant, and diffuse perspiration may occur. Nausea and vomiting are also frequently noted as the fibers in the second lobe are cut. Urinary incontinence may be noted directly after lobotomy — a complication most troublesome to nurses. Inadequate control of anal sphincters, on the other hand, rarely occurs. Soon after operation many patients show markedly increased appetite and gain in weight. For a few days after lobotomy, the patient may be in bed in a "drowsy-anergic" state, usually motionless, but capable of brief arousal by stimuli to which he may even appear hyper-reactive.[150]

Lyerly had one hypertensive patient whose blood pressure fell to normal and remained normal. Freeman had 3 hypertensive patients who showed prolonged lowering of the blood pressure after lobotomy. Chapman and his associates[151] have very carefully studied both normotensive and hypertensive patients before and after lobotomy and have described a lowering of blood pressure, greater in hypertensive than in normotensive persons, with a gradual return to preoperative levels within three months. Statistical evaluation failed to reveal a significant difference in preoperative and post-

operative blood-pressure levels when sufficient time was allowed for recovery from the traumatic effects of the operation.

The cause of the increase in appetite and weight is not thoroughly understood. Some are inclined to attribute the phenomenon wholly or in part to loss of tension, increase in contentment and self-satisfaction — that is, removal of cephalic inhibitions to eating. Improvement of gastrointestinal function has also been invoked to explain the phenomenon, for indigestion, dyspepsia and peptic ulcer are generally relieved postoperatively.

The explanation of the phenomenon of urinary incontinence has received some attention. Generally the wetting is attributed to indifference, apathy and neglect. It is found more commonly in the disorganized, deteriorated patients than in those who are well preserved. Rinkel, Rosen and Levine[152] have made important observations bearing on the mechanism of wetting. They have shown that after lobotomy the bladder is often contracted, and the capacity low.

Members of the Boston Psychopathic research group (Rinkel et al.[153-155]) have attempted to appraise the stability or instability of the autonomic nervous system by response of the adrenergic or cholinergic system to specific stimulation. After operation patients with chronic schizophrenia showed a more pronounced blood-pressure and pulse-pressure rise to intravenous administration of epinephrine than that before operation. The carotid-sinus reflex, too, appeared to be more responsive to stimulation, for cardiac slowing and asystoles were more common after operation than before. The data were taken to indicate that the autonomic nervous system was for a time released from higher control by lobotomy.

After operation the patient is frequently hyperreactive to many stimuli, often shrinking back from physical contact. Nurses find it difficult to take rectal temperatures, give baths or change head dressings. Removal of sutures is often violently resisted, and a very exaggerated reaction may accompany a venipuncture that was preoperatively accepted as routine. This reaction tends to be worse if the patient is allowed to anticipate the pain or discomfort.

Personality Changes After Lobotomy

Is there a lobotomy personality? Earlier in the history of psychosurgery it was feared that lobotomy would reduce the patient to vegetable status; however, experience has taught that although considerable alteration may occur in the individual pattern, the core of the personality remains much the same — usually, to paraphase Moniz, "there are no grave repercussions" in the part of the personality. Furthermore, the total personality constellation may change to a more wholesome adaptive type in which disorganizing fears, obsessions, anxieties and even delusions and hallucinations have been mitigated or lost.

Widening experience leads one to a profound respect for the heterogeneity of personality modifications resulting from lobotomy. Quite opposite personality changes may, for example, be affected in patients who before operation presented similar psychoses. In some persons aggression may be allayed by lobotomy; in others, aggression may be released by lobotomy — what transpires apparently depending upon how the frontal association areas served the patient in question.

Changes of personality after lobotomy may be discussed under the following headings:

Drive. This aspect of the personality is usually, but not always, represented as being reduced. Thus, various authors speak of a postlobotomy apathy,[70, 110] laziness,[156, 157] lack of initiative,[70, 82] loss of spontaneity,[35] indolence,[10] lethargy, reduction of active reactions to passive ones[111] and somnolence, particularly in the immediate postoperative period. Ambition and goal-directed enterprise are often wanting, being replaced by contentment with a matter-of-fact, simplified existence.[156, 157] On the other hand, the drive may be taken out of suspicious, hostile and aggressive attitude; the delusional or distorted fantasy life of the patient may be gradually uncharged, or episodes of unbridled violence may be muffled, allowing the patient to be tolerated among his fellows. Some patients, quite contrary to the general run, after lobotomy take up life with renewed vigor and return to challenging occupations with diligence and industry.

Self-concern. Perhaps the most specific functions of the personality attacked by lobotomy are those that relate to anxious self-concern and uneasy self-preoccupations. Tension, agitation, obsessive brooding,[83] self-consciousness, shyness,[121] and excessive reserve are reduced. The patient is often less sensitive to criticism, rebuke or scorn.

Outwardly directed behavior and social sense. The patient is usually more accessible, for his energies are no longer so closely tied up with himself. He may turn his attention more toward reality, take notice of external influences and conditions, behave more appropriately in the group, seek out and enjoy others and no longer actively retreat from social intercourse. In his social relations, however, he may lack tact and diplomacy, may be abrupt in manners and speech, speak his mind without concern for the remote possibilities of his actions and make quick decisions without the advantage of deliberation. However, antisocial or amoral behavior has not been a conspicuous problem among lobotomized patients, and behavior is usually well within the bounds of the patient's former moral code.

Affectivity. Although disabling depression, anxiety, and agitation are relieved, the patients may pay for the relief — in bilateral lobotomy, with a more superficial or shallow affective life.[158] Buoyancy and euphoria may result, particularly from the orbital operation.[80] In addition, some patients display irritability and aggressiveness, and a sudden flaring up of temper may occur when they are frustrated, with just as sudden cooling down; after the explosion, the patient is usually incapable of keeping alive a grudge.

Sexual Behavior after Lobotomy

Sexual behavior in the majority of cases does not seem to undergo any great alteration, according to Freeman and Watts.[159] Postoperatively, inertia may reduce the tendency toward gratification; on the other hand, the suppression of restraining forces may lead to freer expression along sexual lines. Lack of self-depreciating ideas permits normal appetites to emerge. Thus, the sex adjustment of married partners may sometimes be improved, and in some cases there is a return of sex interest that has been dormant for months or years prior to operation. The attitude toward sex is more objective and matter-of-fact; the patient may be less modest, unabashed or frankly outspoken. Only a few cases of exaggerated sexuality are recorded by Freeman and Watts, and no cases of sexual perversion or socially offensive conduct. Hutton has seen no antisocial or amoral behavior. McKenzie and Proctor,[90] however, state that 25 per cent of their cases showed "hypersexuality" with return to normal in nine to eighteen months.

Levine and Albert[160] studied 40 co-operative patients who had improved clinically after lobotomy and were functioning in their own homes. In general, a decrease in sexual drive and in degree of gratification in sexual experience was noted. The intensity of pleasure accompanying the sexual act was usually less. Interpretation of this phenomenon was difficult in view of the long duration of illness and hospitalization of some of the patients with either abstinence or lack of normal gratification during that period. The dream and fantasy life was apparently impoverished. In a few cases sexual activity was increased, and some patients who had previously been inhibited for long periods became sexually interested. Two patients were excessively demanding after operation; one was an elderly gentleman who wearied his wife because of his abnormal appetite and "staying" power; the other was a young unmarried man who before operation was an inhibited obsessive-compulsive, and who afterward indulged lustily in both sex and drink and boasted of his prowess. Levine and Albert were impressed with the fact that sexual behavior after operation was generally kept well within the patient's moral bounds.

Rehabilitation

Impressed with the hypothesis that after lobotomy there is a new opportunity to crystallize personality organization into a more wholesome pattern, many workers have stressed the importance of proper rehabilitation programs designed to promote the full growth potentialities of each patient after operation. The great difficulty has been selecting programs properly individualized for each patient.

Immaturity, child-like behavior, lack of initiative and procrastination[9, 10] are traits that have to be dealt with during the rehabilitation period. Suggestibility, lack of emotional restraints, greater interest in environment and less resistance to socializing are traits that favor progress in rehabilitation.[89] The necessity of beginning the work of readaptation as soon after lobotomizing as possible is emphasized by Whitman,[161] Ewald et al.,[162] Farmer[163] and others. Prolonged convalescence in the hospital, where rehabilitation can be carefully managed, rather than early discharge to an unorganized environment is favored, particularly by the English group of workers (Frankl and Mayer-Gross[164] and Fleming[89]). Early discharge to the family may be attempted only when the relatives are mature with wholesome attitudes toward the patient,[24, 161, 165] and when adequate supervision can be exercised at all times. Families should be chosen as carefully as patients, according to Watts[9]; Fleming[89] asserts that rehabilitation and re-education are the most important part of the whole treatment program. Readjustment and reintegration of the lobotomized patient may continue for three to five years. The rehabilitation period is therefore extremely long by any ordinary standards; hence, both long-range and short-range planning programs become a necessity.

During the rehabilitation period electric-shock and insulin-shock therapy may be used with success, even though the patient may have failed to respond to these procedures prior to operation (Whitman,[161] Fernandes[166] and Schrader and Robinson[167]). Schrader and Robinson[167] state that electric shocks given after lobotomy appear to shorten the period of recovery and augment favorable results. Freeman and Watts[9] used electric-shock therapy after lobotomy, particularly when improvement was followed by relapse.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 35251

PRESENTATION OF CASE

A thirty-nine-year-old Russian-born man, a clerk, entered the hospital because of malaise and low-grade fever.

Twenty-six years before admission, at thirteen years of age, the patient had an attack of rheumatic fever for which he remained in bed for ten days. Twenty years before admission he had another attack of arthritis. He first noted dyspnea on strenuous exertion eighteen years before admission and occasionally he spat bloody material. In that year he had an episode of acute failure after swimming half a mile. Subsequent examination revealed an apical diastolic murmur, and on x-ray study the left ventricle was enlarged. He gradually restricted exercise and was comfortable except for occasional periods of hemoptysis, often, but not always, brought on by exertion. He had pneumonia twice and numerous upper respiratory infections. About nine years before admission while doing only light office work he complained of insomnia that was due mostly to dyspnea. He had a long-drawn-out, rumbling diastolic murmur at the apex, with a presystolic accent transmitted along the sternal border. Six years before admission the patient developed grippe and enteritis and thereafter had progressive muscular weakness that incapacitated him. Severe breathlessness, sometimes in attacks, and insomnia were prominent. The liver was palpable and tender. There was no ankle edema. The diastolic murmur was much louder. An electrocardiogram four years prior to admission showed auricular fibrillation with partial auriculoventricular block and a heart rate of 50. He had been taking digitalis and doses of ammonium chloride for several months. Following readjustment of the dosage of digitalis the muscular weakness disappeared, and the heart rate increased. He was able to work about twenty hours a week with infrequent exceptions from that time until the episode of fever. One month before admission the patient had a tooth extraction. He then developed malaise, anorexia, loose bowels and a temperature varying up to 100.6°F. These symptoms, in addition to marked weakness, persisted until admission. The chronic cough and dyspnea continued. Small amounts of white sputum were raised. In the three days preceding admission he had generalized aches and severe bilateral calf pain. An x-ray film taken outside the hospital the day before admission was said to have shown pulmonary infarction. Four blood cultures taken during the present illness were said to have been negative.

Physical examination showed an orthopneic and mildly cyanotic man breathing at a rate of 36 per minute. The neck veins were prominent. Over the right lower and middle lobes resonance was impaired, and voice and breath sounds were increased. Many crackling rales were present, and expansion on that side was limited. The apical beat was maximal in the sixth interspace 7 cm. to the left of the midsternal line. The heart was enlarged, the border of cardiac dullness extending to the right. It had an irregular rhythm, with an apical rate of 96 and a radial rate of 88. The first sound at the apex was very forceful. There were Grade II apical systolic and diastolic murmurs. The pulmonic second sound was greater than the aortic second sound. The abdomen was distended, and the spleen and liver were palpated 3 and 7 cm. respectively below the costal margins; both were tender. There was moderate edema of the ankles. The calves were tender. Homans's sign was negative.

The temperature was 100.5°F., and the blood pressure 136 systolic, 88 diastolic.

Examination of the blood disclosed a hemoglobin of 15.5 gm. and a white-cell count of 16,700, with 88 per cent neutrophils. The urine had a specific gravity of 1.018 and gave a +++ test for albumin; the sediment contained numerous hyaline and granular casts. An electrocardiogram revealed auricular fibrillation, with a ventricular rate of 110 to 120. There was moderate right-axis deviation; the ST segment sagged in Leads 2 and 3. A blood culture was negative. Injection of penicillin was started on the first day. The superficial femoral veins were ligated on the second hospital day. No clot was found. Over the course of several days there was a steady increase in the severity of the patient's illness. He became more cyanotic; the heart rate increased despite continued digitalis, and the pulsations became weaker. On the third hospital day the nonprotein nitrogen was 52 mg. per 100 cc. The temperature returned to normal. Slight jaundice appeared. By the seventh hospital day he was weak and restless. The icterus increased. The nonprotein nitrogen was 106 mg. per 100 cc., and the carbon dioxide 13.1 milliequiv. per liter. During the last twenty-four hours there was no urine output. The radial pulse and the blood pressure were unobtainable. The patient died on the eighth hospital day after being in coma twenty-four hours.

Differential Diagnosis

Dr. T. Duckett Jones: Since the age of twenty-one this case had been a problem of clear-cut, severe rheumatic heart disease. We have in a large follow-up group a reasonably large number of persons with severe heart disease, all of them with mitral stenosis, who are blood spitters. They do not necessarily at the time have any evidence of pulmonary edema or any evidence of pulmonary infarction, but over a period of years at frequent intervals they spit blood. The great majority of them have no evidence of active rheumatic fever. Many of them have been studied both in the hospital and outside with regard to x-ray examination of the chest, white-cell count, sedimentation rate and electrocardiograms. They have always been essentially normal so far as anything indicative of active rheumatic fever is concerned. The actual basis for the blood spitting can be explained much more accurately by Dr. Mallory, but I would assume it was on the basis of extensive changes in the pulmonary vessels, which have been mentioned by a number of observers in the past, particularly Parker and Weiss.[1]

I am surprised that no mention is made of the left auricle in the x-ray examination, because I think he must have had mitral stenosis. What the two attacks of pneumonia mean, I do not know. Whether it was really lobar pneumonia or pneumococcal infection is questionable. The rheumatic patient, however, does have attacks of pneumonia at times and for some strange reason over a period of years has survived them quite well, even before the days of modern therapy.

Obviously, this man had real mitral stenosis. I do not know what the relation between the so-called grippe and his decreasing cardiac reserve was. I doubt very much if it meant that he had active rheumatic fever, although that is a possibility. The liver was palpable and tender on examination in the Out Patient Department — four years before his final admission, so that he is known to have had failure for a long time.

The calf pain, I think, is possibly the first evidence that this man may have had bacterial endocarditis, and I raise the question immediately whether or not he was having emboli. It is obvious that he was considered as a possible or probable case of bacterial endocarditis at the time of the hospital admission.

"The apical beat was maximal in the sixth interspace, 7 cm. to the left of the midsternal line." I would strongly question that measurement, because it is rather obvious that the patient had a very extensive cardiac hypertrophy and I believe that most sixth-interspace hearts are well out and not 7 cm.

The heart "had an irregular rhythm, with an apical rate of 96 and a radial rate of 80." I think that indicates that he had definite fibrillation, which shot his rate up on partial digitalization, but I somewhat doubt this because his previous difficulty was too much digitalis. I assume that the presenting feature of a mitral diastolic murmur had disappeared with the onset of auricular fibrillation; it is customary but not 100 per cent so. There is nothing in the description of the murmurs to indicate aortic as well as mitral disease, but most patients with rheumatic heart disease, with an impulse in the sixth interspace, have some aortic as well as mitral disease. I therefore think that he also had some aortic disease, although the description of the murmurs is not sufficient to make that a definite diagnosis.

The enlargement of the liver is to be expected because he had obvious cardiac failure. The cause of the splenic enlargement will be mentioned later. Both liver and spleen were tender, which might mean that he had splenic infarcts; I am not sure. Engorged livers are usually tender. It is perfectly obvious that whoever examined him was thinking in terms of the leg veins as a possible source of his trouble — a pulmonary infarct that happened a day or two prior to admission.

The blood picture was probably on the side of infection.

I believe it is likely that these urinary findings were of more importance than the ordinary urinary findings that one sees in congestive heart failure — more of that later.

There was some concentration of the nitrogenous products, and, of course, the carbon dioxide was reduced by more than 50 per cent.

The first thing to decide now is whether or not he had bacterial endocarditis superimposed on his rheumatic heart disease. He lived only about five weeks after the tooth extraction, and yet apparently he had been in no very different status in the few months prior to that extraction. In addition, the short duration would make it necessary for the endocarditis to have been an acute process, and the course was not that of acute bacterial endocarditis — that is, a high, striking temperature, usually with chills, and a rapidly progressive septic course. There was no sepsis, no fever, no chills, and no bacteria, which is somewhat against bacterial endocarditis, and the course was short for a subacute process. He had no positive cultures, which is evidence against subacute bacterial endocarditis but does not necessarily rule it out. In addition, he had real mitral stenosis, and it is unusual to have bacterial endocarditis on a severely damaged valve. Of course he may have had mild aortic disease, and the bacterial vegetations may have been placed there. Since no note was made that confirms aortic-valve involvement, and since he did have severe rheumatic heart disease, with real mitral stenosis, and auricular fibrillation, I submit that he did not have bacterial endocarditis.

We have a great many things to explain on some other basis. What was the mechanism of the cardiac failure? Did he have sufficiently severe rheumatic heart disease to fail without any additional factor? We know that this occurs in adults. He had had failure off and on for eighteen years, so that I assume he had enough rheumatic heart disease to fail without very much in the way of active rheumatic fever. Also, I believe that he had kidney changes sufficient to cause some additional burden to the circulation. A good many patients with acute nephritis have heart failure, so that from the evidence it is possible that the nephritis had more effect on the terminal episode than actual rheumatic fever.

Did he have nephritis? He had retention of proteins. He also had jaundice. Do we have to make two diagnoses? Since rheumatic fever and glomerulonephritis can occur together and since they both have the same background of streptococcal infection, I am willing to believe that this man did have nephritis at the end, and that it played a definite role in his picture. I do not believe that bacterial endocarditis could be responsible for his nephritic picture. At least the patients that I have seen who died in uremia with bacterial endocarditis did so only after a long drawn-out illness.

We also have to explain the pulmonary picture. I suppose we should have looked at the x-ray films. We will come to them in a few minutes. I do not believe that we have to predicate the presence of thrombophlebitis in the legs to account for the pulmonary picture. Patients with failing rheumatic hearts often have pulmonary infarcts, but they can develop on the basis of disease in the pulmonary arteries rather than on the basis of embolism from the periphery of the body.

Did he have active rheumatic fever? Tooth extraction is known to stir up active rheumatic fever at times, and he did have a low-grade fever. He had an elevated white-cell count and had had at least two or three frank bouts of active rheumatic fever. If one exhaustively sectioned the heart muscle one might find Aschoff bodies or evidence of active rheumatic fever. However, it seems more likely that the additional nephritic burden, which I believe was present here, was sufficient to account for failure without an appreciable degree of active rheumatic fever. So I should like to guess that this man, who had severe rheumatic heart disease and mitral stenosis, also had glomerulonephritis, and that the severity of the rheumatic heart disease and the additional nephritic burden was sufficient to cause the entire syndrome that ended fatally.

Perhaps we should see the x-ray films.

Dr. James R. Lingley: The heart shadow is grossly enlarged even though the film was taken with a portable apparatus at close distance. There is prominence to the right of the spine and marked prominence to the left in the region of the left auricle. The pulmonary artery is enlarged, and there is some enlargement of the vessels throughout both lungs. In the left side there is a small quantity of fluid along the axillary border. On the right side there is a large, sharply defined shadow at the base, which in the lateral view is in the midchest, in the anterior portion of the lobe, and is consistent with infarct.

Dr. Walter Bauer: Are we justified in making a diagnosis of glomerulonephritis without the presence of red cells in the urine?

Dr. Jones: We have only one analysis but he may have had red cells at another time.

Dr. Bauer: Jaundice occurs with pulmonary infarction, with congestive failure; perhaps the slight jaundice could be accounted for on that basis.

Dr. Jones: It has always been surprising to me that one does not get more jaundice in terminal rheumatic heart disease because the amount of liver change is tremendous.

Dr. Bauer: You would not be satisfied to say that the renal findings contributed by the laboratory studies could be adequately explained on the basis of congestive failure, phlebitis and pulmonary infarction.

Dr. Jones: I do not believe that as a rule the rheumatic patient develops uremia as a simple consequence of failure.

Dr. Chester M. Jones: In a few young persons we have seen definite jaundice without pulmonary infarction but with marked changes in the liver.

Dr. T. Duckett Jones: There have been three or four such cases. We have never been able to explain them other than on the basis of rheumatic fever causing liver change.

Clinical Diagnoses

Rheumatic heart disease, with mitral stenosis.
Auricular fibrillation and congestive failure.
Pulmonary infarction.
Pneumonia.

Dr. Jones's Diagnoses

Rheumatic heart disease, with mitral stenosis.
Glomerulonephritis.
Pulmonary infarction.

Anatomical Diagnoses

Rheumatic heart disease, with mitral and aortic stenosis.
Periarteritis nodosa of lungs.
Organized pneumonitis.
Hepatic cirrhosis.

Pathological Discussion

Dr. Tracy B. Mallory: Autopsy showed, as Dr. Jones predicted, very severe rheumatic heart disease. The mitral valve was reduced to a narrow slit, and the aortic valve was markedly stenotic. As he pointed out, the real question in the case was the

nature of the acute terminal episode. It was not a glomerulonephritis. The kidneys showed only relatively mild tubular degeneration, which, I think, can be adequately explained as secondary to the other findings.

The surprise of the autopsy was provided by the lungs. Both lower lobes and the middle lobe on the right were very firm and heavy and cut with the consistence of leather. Even the two upper lobes were distinctly fibrotic. We were still further surprised when the microscopical sections came through. This photomicrograph (Fig. 1) shows one of the medium-sized pulmonary arteries. The lumen is almost completely occluded by thrombus. The media has been completely destroyed and appears dense black in the picture. Around the outside of the artery is an inflammatory infiltration consisting largely of lymphocytes. The small branches

FIGURE 1.

of the artery show the same picture: complete necrosis of the media, periarterial inflammation and thrombosis. The second slide (Fig. 2) is an example of the fibrotic pulmonary tissue and could have been taken from any one of the three lobes. The lumens of the alveoli are lined with apparent epithelium. The alveolar walls are five to ten times as thick as normal, and the respiratory function must have been reduced by 75 per cent. The puzzling picture is that the pulmonary fibrosis looks old, whereas the arterial changes are for the most part quite recent. There are a certain number of vessels scattered throughout the lung that show older changes. None of them impressed me as being of more than a few months' duration. In contrast, this diffuse fibrosis is apparently a process of several years' duration, tracing back, I should think, to some of the episodes of pneumonia. I would inter-

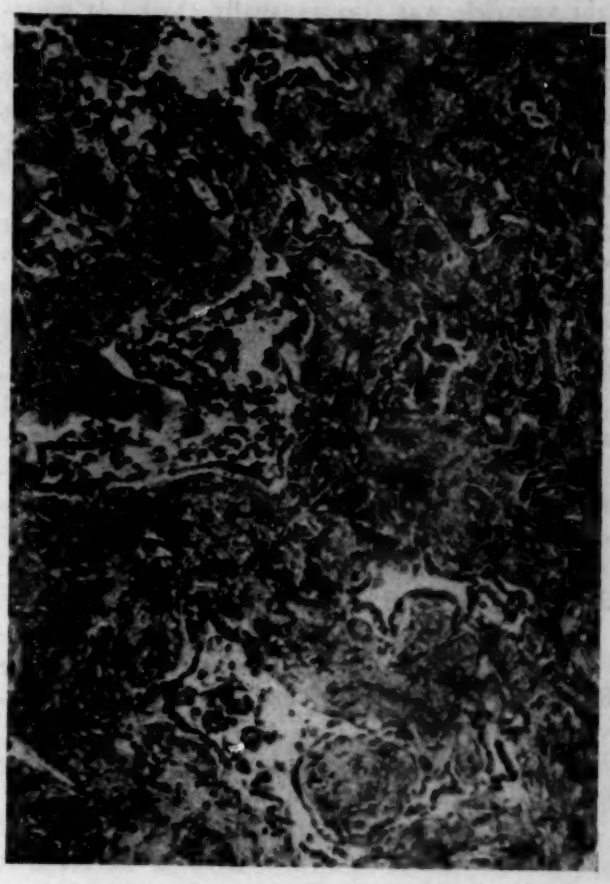

FIGURE 2.

pret them as organized pneumonia or pneumonitis. Another possibility is a healed interstitial pneumonia.

What are we going to call this? What are the arterial lesions? The histologic appearance of the individual lesion is essentially that seen in so-called periarteritis nodosa. On the other hand, many sections from all other organs in the body completely fail to show similar lesions. The vascular process was entirely restricted to the lung. The heart showed only completely healed endocarditis of the valves. There was no trace of activity in the myocardium. We have gradually become conscious in the last few years that periarteritis nodosa, so called, is not a specific disease but is simply a reaction pattern that can develop from a variety of etiologies. This case presents lesions anatomically entirely similar to periarteritis but limited to one

organ in the body. It could be considered evidence of acute rheumatic infection, but we have no confirmation.

There was one additional finding of some interest. The liver showed a very well developed cirrhosis such as can occur in chronic rheumatic heart disease, but it seemed to me more marked than that ordinarily seen in this degree of mitral stenosis. The right ventricle was also unusually thick. It measured 1 cm. in thickness compared with a left ventricle of only 1.4 cm. I think that without much doubt the pulmonary lesion considerably increased the strain on the right ventricle, beyond what could be explained by the mitral involvement.

DR. JONES: Would you think the pulmonary lesions, the acute ones, were comparable to Rich's[2] sulfonamide cases?

DR. MALLORY: Yes; they are perfectly consistent with that.

DR. JONES: I do not know whether this patient had sulfonamide prophylaxis at the time of death.

A PHYSICIAN: He did not develop signs of consolidation in the right lower lobe until two days before coming to the hospital.

DR. MALLORY: We found nothing to explain that. All the lesions there are of years' duration.

DR. JONES: Would you agree that these changes — if they are to be considered as evidence of active rheumatic fever — would call for a complete re-evaluation of what we term active rheumatic fever, on the basis of the findings that we see in the younger person? One does not find this pattern very often.

DR. MALLORY: No; there are occasional cases of active rheumatic fever with arteritis so severe that one begins to think of calling it periarteritis nodosa, but these cases are the exception.

DR. BAUER: Would the roentgenologist be able to read this chest plate differently now?

DR. LINGLEY: I am afraid not. I do not understand what the shadow in the right lower lobe could be.

DR. BAUER: Are you wholly satisfied with the explanation of the pulmonary changes?

DR. MALLORY: As a healed pneumonitis?

DR. BAUER: Yes.

DR. MALLORY: I think there are two alternatives, either healed pneumonitis or the scars of long successions of pulmonary infarction. I am rather sure that one can rule out the latter.

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CASE 35252

PRESENTATION OF CASE

A sixty-nine-year-old divorced woman was admitted with the complaint of an abdominal mass that had been increasing in size over a period of seven years.

When first detected it was said to have been the size of a walnut, located in the left lower quadrant and without associated symptoms. About three years before admission the mass had increased markedly in size and the patient began to notice increasing urinary frequency, nocturia and anorexia. At the same time she began to notice a tendency to bruise easily. She had some discomfort when erect, and difficulty in sleeping required medication from her physician. As the mass increased in size she developed moderate dyspnea and some palpitation on exertion, for which she was given daily green pills. At the time of admission, almost the entire abdominal cavity had become filled with the mass. She had lost 30 pounds during the previous three years but denied nausea, vomiting or change in bowel habits. There apparently had been no vaginal bleeding since the menopause at the age of fifty-three.

Twenty-nine years before admission she had an episode of post-partum phlebitis in the left leg and had recurring ulcerations about the left ankle. About twenty-five years before entry she had an episode of severe hemorrhage following multiple tooth extractions.

Physical examination revealed an emaciated, elderly woman with bronze pigmentation of exposed skin areas and multiple ecchymotic spots over the arms and upper trunk. Her color was high but not violaceous. A few telangiectases were present over both cheeks and the right ear. The heart was somewhat enlarged to percussion. There were frequent extrasystoles occurring irregularly and a Grade I, precordial systolic murmur. The aortic second sound was greater than the pulmonic. There was some dullness to percussion, and decreased breath sounds with fine crepitant rales at both lung bases. A large, smooth, hard mass filled almost the entire abdomen except for a portion of the right upper quadrant. It was not easily movable but was not attached to the abdominal wall. A definite notch was palpable on its right border below the level of the umbilicus. It was not palpable rectally, and the pelvic examination was within normal limits. The liver edge was palpable about four fingerbreadths beneath the costal margin in the right flank. A few small soft and nontender lymph nodes were palpable in the inguinal and cervical regions bilaterally. There was some distention of superficial veins in the neck and left leg. Slight edema, skin pigmentation and old scar formation were present about the left ankle.

The blood pressure was 148 systolic, 90 diastolic.

Examination of the urine was negative. The white-cell count was 23,850, with 87 per cent neutrophils, 3 per cent lymphocytes, 2 per cent monocytes, 1 per cent basophils and 7 per cent young forms. The granulocytes showed a shift to the right. The red-cell count was 8,260,000, and the hemoglobin was 18.5 gm. per 100 cc., with a hematocrit of 76 per cent. The red cells demonstrated considerable variation in size and shape with some achromia, many cells showing polychromatophilia. The reticulocyte count was 7 per cent, with occasional normoblasts. The platelets were diminished. The sedimentation rate was 0. The bleeding time was 1.5 minutes and the clotting time 11 minutes. The prothrombin time was 57 per cent of normal. The plasma fibrinogen was 0.25 gm. per 100 cc. A stool was soft brown and guaiac negative. The nonprotein nitrogen was 34 mg., and the total protein 6.2 gm. per 100 cc., with an albumin-globulin ratio of 2.5; the serum calcium was 8 mg., the phosphorus 3.5 mg., and the alkaline phosphatase 5.9 units per 100 cc. The serum chloride was 102 milliequiv. per liter. The van den Bergh reaction was 1.0 mg. per 100 cc. direct and 1.4 mg. indirect. The cephalin-flocculation test was 1+ in forty-eight hours. The thymol-flocculation test was negative. The thymol turbidity was 4.0 units. The bromsulfalein test showed 5 per cent retention of the dye in forty-five minutes. An electrocardiogram was defined as a normal tracing. The basal metabolic rates on two occasions were +69 and +59 per cent.

X-ray examination of the chest revealed some prominence of the cardiac shadow in the region of the left ventricle, with an elongated tortuous and partially calcified aorta. The lung fields were bright, with generalized prominence of the pulmonary markings. A plain film of the abdomen showed generalized decalcification of long structures, with collapse of a number of the ureteral segments. A large soft-tissue mass filled the left side of the abdomen and pelvis, with several flecky areas of calcification in the left pelvis. A dense linear streak of calcification in the left pelvis was thought to represent a calcified thrombus in the left iliac and femoral veins. Excretory urograms showed moderate embarrassment to drainage bilaterally but demonstrated no definite relation between the upper urinary tract and the abdominal mass. A barium enema revealed downward displacement of the major part of the colon by an extrinsic mass, but no intrinsic lesion was seen.

The patient was afebrile throughout the course of study in the hospital. On the seventh hospital day a sternal-bone-marrow aspiration was performed and reported as showing a myeloid-erythroid ratio of 9:1, with a marked shift of myeloid maturation to the right. No blast forms were seen, and there were rare premyelocytes. Megakaryocytes were plentiful. No plasma cells were seen. On the fourteenth day a sternal-marrow biopsy was performed, and marrow imprints were reported to show a myeloid-erythroid ratio of 6:1, with normal cells and increased megakaryocytes. On the following day the patient developed a painful subpectoral hematoma in the region of the biopsy site. Subsequently, she complained of mild perspiration and chilly sensations, with pleuritic pain over the right lower chest posterolaterally. There was no cough or hemoptysis, but there was slight tenderness in the left calf and thigh. On the seventeenth hospital day while elevating her arms for an x-ray examination of the chest, she experienced sudden pain in the left anterior chest and subsequently noticed rather rapid increase in size of the hematoma with extension over the chest and posteriorly. Subsequently, she developed rather severe hypotension and a feeble pulse, with a radial rate of 130. Intravenous injection of protamine and intramuscular administration of vitamin K were given in addition to fluids intravenously and sedation. On the following day, the subpectoral hematoma was evacuated under local anesthesia. Postoperatively she had a pulse rate of 150, but the blood pressure was not obtainable. She was drowsy but responsive and coherent. There was no cyanosis.

On the nineteenth hospital day she developed dyspnea of progressive severity and abdominal distention with ileus and died quietly and abruptly the same evening.

Differential Diagnosis

Dr. Joseph C. Aub: The description of the mass is important because the description of a tumor low in the abdomen suggests a tumor in the ovary, but there was no history of recent vaginal bleeding.

The chest findings mean nothing but congestion of the lungs; they do not imply fluid.

There are only three reasons for the slowed prothrombin time: a vitamin K deficiency, liver damage or the eating of red clover. There is no history of the eating of red clover, which is used as a treatment for cancer by traditional American folklore. Perhaps the patient was taking red-clover tea. The albumin-globulin ratio showed a relatively reduced globulin. The liver was large. The phosphatase was a little high. All this is hard to interpret but suggests diminished liver function.

It is interesting, but not exciting, that the basal metabolic rate was elevated because it may be quite high in both leukemia and polycythemia.

So far, I should say that this patient had polycythemia vera, because the white cells were mature. Why the platelets were diminished is not clear.

It will be very interesting to see if the x-ray films show a great deal of emphysema. This might account partially for the polycythemia, and I would like to find some reason for anoxia. It is interesting that in polycythemia, one gets decalcification of

the vertebras, where a great deal of blood is made, and where the bone is composed largely of trabeculae that may become so thin that vertebral collapse may result.

The x-ray findings establish the fact that this mass was the spleen and not the kidney. If it were kidney or a retroperitoneal mass, the large bowel would be pushed over and not pushed down by it. It is only the spleen that pushes the large bowel ahead of it.

The bone marrow contained an enormous number of white cells. Dr. Jacobson says the normal ratio is 4:1 to 8:1. Certainly, with polycythemia vera there should be many more red cells than white cells. This is a high number of white cells for polycythemia but does not rule it out. There were very few platelets in the circulating blood, and yet many megakaryocytes were present in the bone marrow. No plasma cells were seen. We must think of multiple myeloma, in spite of this fact and the normal total protein and low globulin in her blood; but it is unlikely.

The first part of this case is, I think, easy. The second part is very befuddling. I do not know just where her pain started, whether this was a pulmonary infarct, or whether it was bleeding with irritation of the pleura. She had tenderness in the calf and thigh, and, I suppose, an embolus was liberated from the phlebitis of the leg.

There is little description of the x-ray examination done at this time — whether it showed evidence of bleeding in the pleura or in the pericardium.

Well, there it is. The mass was the spleen. The diagnosis is polycythemia vera. There are a good many questions in relation to that. Why did she have so few platelets? The blood of polycythemia ought to have many platelets. She had a great many megakaryocytes in the bone marrow but very few platelets in the blood stream. I do not know why. She bled, which is common in polycythemia, and I think she died of bleeding. She had a high white-cell count, 23,800, and all the cells were mature, with no abnormal cells; this is also common in polycythemia. In fact, I recently saw a patient with straight polycythemia who had almost 100,000 mature polymorphonuclear cells. About 10 per cent of patients with polycythemia have leukemia as they progress. But I do not believe that this patient had leukemia.

I see no good evidence for the diagnosis of agnogenic myeloid metaplasia. Incidentally, this disease interests me very much as a preneoplastic lesion. This disease is a beautiful example of an enormous, increased production of red cells. Why it causes an increased production of normal adult red cells and then ends up with a neoplasm is fascinating; there is no explanation for it that I know of, and it remains an interesting opportunity for the study of preneoplastic lesions.

I want to see the x-ray films.

Dr. Joseph Hanelin: I believe she has an emphysematous chest. The anteroposterior chest diameter is increased, and the sternum bulges forward.

The first set of chest films, taken on the second hospital day, shows findings in the chest essentially as described. The heart is somewhat enlarged, and the left ventricular salient is prominent. There is calcification of the aorta. In the lateral film of the chest multiple vertebral fractures involving the lower thoracic and upper lumbar segments are visible. There also appears to be a rib fracture on the right. The left costophrenic sulcus is blunted. One wonders whether this might be due to underlying infarct or whether it is possibly of longer duration, owing to some thickening of the pleura.

On the sixteenth hospital day, the chest findings have changed slightly — at least, to demonstrate very nicely the large subcutaneous hematoma, which is now visible anterior to the sternum. I rather suspect that the density noted overlying the left portion of the thorax is also due to subcutaneous blood accumulation. There is a small amount of fluid in the right costophrenic sulcus, possibly related to the rib fracture.

The plain abdominal film confirms Dr. Aub's impression that he was dealing with an enlarged spleen. There is a large mass in the left abdomen of ovoid configuration. The normal splenic shadow cannot be seen. I assume this is an enlarged spleen. In addition, the lower edge of the liver is situated below its normal location and extends slightly below the iliac crest. Pyelograms show slight embarrassment to drainage on the right and a slightly hydronephrotic renal pelvis on this side. Renal function may be impaired somewhat bilaterally. In the abdominal film there is a calcified streak following the course of the left iliac and femoral vein, which probably represents a calcified thrombus. In the anteroposterior view, we can also note the fracture of the lumbar segments. All the bones are decalcified, but in a woman of this age, the degree of osteoporosis is not unusual.

Dr. Aub: The emphysema does not help me because it is not sufficiently marked. I do not think this patient had kala-azar, or myeloid metaplasia. She had polycythemia, as I said before, and I think polycythemia vera. So far, I am sure that I am on firm ground. From here on, I am on less firm ground because I do not know whether the hemorrhage killed her, or an infarction. Patients with polycythemia have hemorrhages, — this patient had had hemorrhages for a long time, — and they bleed very heavily, just as patients with leukemia do. This patient also had few platelets and a slow prothrombin time. Also, in polycythemia thrombi develop, and they may get loose. This woman died in shock, and she died while she was bleeding. Therefore, it seems to me, she died of either hemorrhage or infarction. The sternal biopsy may have gone

through into the upper mediastinum, and may have extended into the pleura, and hemorrhage may have occurred in the pericardium with subsequent cardiac tamponade. I have not enough evidence to say whether these occurred. She had some suggestion of phlebitis in her leg. There is evidence of old phlebitis. She had a sudden sharp pain in the chest, though she did not cough or spit up blood. She may well have had a pulmonary infarct, sufficiently great to cause anoxia, shock and death. She may possibly have had a cardiac infarct.

I have not enough evidence to make a differential diagnosis. I have some evidence that she was bleeding and some evidence that she had cause for having a large pulmonary infarct; no evidence is given that she had a cardiac infarct. I know she was bleeding about the sternal biopsy, and these people do go into shock from hemorrhage, and I believe that she kept on bleeding, with extension into some cavity, either pleural or pericardial. I rather guess that she had a large pulmonary infarct from which she went into shock and died. Therefore, I should be surprised if she did not have polycythemia vera, and I do not expect myeloid metaplasia or neoplasm in the bones. Her thin bones were due to the fact that they were full of actively regenerating blood and that the trabeculae had been hollowed out by this long, slow disease. I think her large spleen was due to polycythemia. Then it is to be expected that the liver has areas of regeneration of red and polymorphonuclear cells, with some hemosiderin in her liver, and probably in her spleen.

Dr. Bernard M. Jacobson: Is there any record of the red-cell count and the hemoglobin in the last few days of life?

Dr. David G. Freiman: Do you know, Dr. Milam?

Dr. Daniel F. Milam, Jr.: She had severe hemorrhage; on the following day the hemoglobin was 17.8 gm.

Dr. Francis T. Hunter: I saw the patient for about two minutes before she was transferred to the surgical department for biopsy. I never saw her again. There was evidence at that time that she had an enormous spleen. Because of the immature white cells in the smear, I thought she might belong to the small group we have seen in the clinic that we cannot make up our minds whether to call polycythemia vera or leukemia with polycythemia. Those with enormous spleens have a relatively benign course, provided they are left alone. Some that we have treated have done very badly. The usual case has a white-cell count of 50,000 to 100,000, with myelocytes and myeloblasts and so forth in the smear. Speaking of polycythemia becoming leukemia, I know of one case of typical polycythemia vera that was treated with "spray" radiation and did well. But after ten years she entered the Baker Memorial with a white-cell count of 150,000, all myeloblasts, and promptly died. Another point that suggests that this case may have been more leukemic than polycythemic — although I admit that I cannot tell where one begins and one ends, or whether they are not one and the same disease — is that the basal metabolic rate was high. In polycythemia the basal metabolic rate is about +25 or +35 per cent; in leukemia it is +70 or 80 per cent. We must remember that this patient had a long history, and, having had no treatment, she could have developed this enormous spleen with polycythemia vera alone. One thing missing in the history is that there is no mention of how long she had the ruddy complexion. Had she been that way all her life?

In regard to the basal metabolic rate, a few days ago I had quite a surprise. At autopsy the patient's spleen was not enlarged but the liver was, and the peripheral blood showed many nucleated red cells and myelocytes. It was my opinion that the high basal metabolic rate (+40 per cent) was in favor of leukemia. Because he was going downhill so rapidly, he was given no x-ray treatment and died soon thereafter. Post-mortem examination showed complete replacement of all the organs with cancer of the prostate. I had not seen such a high metabolism from cancer before, and this was explained by the rapidly growing tumor cells.

As to death from hemorrhages in this case, there is one cavity not mentioned. How about the peritoneal cavity? Could she have had a ruptured spleen?

Dr. Aub: The basal metabolic rate varies with the number of young cells, and in this disease may be due to the high, specific dynamic action of protein. The red cells discard their nuclei, and the uric acid excretion is high, and so there is a high protein breakdown from this disease. Besides, the white cells that were present in this bone marrow could account for some of the high metabolic rate on the basis of rapid regeneration of cells. As far as having bled into the abdominal cavity is concerned, that is possible. I do not know where the hemorrhage gravitated to.

Dr. Hunter: I mentioned that because there was a case of leukemia on the medical ward a good many years ago; the patient squeezed his abdomen hard, went into shock and died. He had ruptured his spleen just by pressing on it.

Dr. Aub: It is not unusual to have the white-cell count as high as this with polycythemia.

Dr. Hunter: That is true.

Dr. Jacobson: I recall asking the patient how long she had had a ruddy complexion. She did not recognize that she had any abnormal high color, and she did not know the answer to that question. The protocol gives no adequate picture of what she looked like. She was one of the most emaciated women that I have ever seen. In addition to the ruddy complexion, she presented a peculiar pigmentation that in the minds of some observers raised

the question of Addison's disease or similar rare conditions. If there is any diagnostic information to be obtained at all from the bone marrow, certainly, in her case, it was not leukemia. The shift was to the right. The white-cell elements were more mature than normal, not less mature, and that is what influenced me mostly in thinking that she was not leukemic, at least, not at that time. It is interesting that on the surgical service she was given intravenous protamine to stop the hemorrhage, with the idea that she had had heparin-like bodies circulating and causing hemorrhage. As I recall, in looking at one of the initial smears, I was not impressed with the diminution in platelets. I do not believe the bleeding was due to thrombocytopenia. I think that anyone who saw her in her fragile, emaciated condition would have been loath to do anything major in the line of surgery on her without some type of treatment directed toward the blood-forming organs.

Clinical Diagnoses

Polycythemia vera.
Splenomegaly.
Subpectoral hemorrhage.

Dr. Aub's Diagnoses

Polycythemia vera.
Hematopoiesis of liver and spleen.
Pulmonary infarct.

Anatomical Diagnoses

Polycythemia vera.
Hematoma, massive, subpectoral and subcutaneous.
Hematoma, slight, mediastinal.
Splenomegaly, marked.
Myeloid metaplasia, spleen and lymph nodes.
Erythropoiesis, focal, liver and adrenal glands.
Pyelonephritis, chronic.
Thrombosis, left iliac and femoral veins.

Pathological Discussion

Dr. Freiman: At autopsy this patient was an emaciated woman with extensive ecchymosis over the anterior thorax, especially on the left, extending up over both shoulders into the neck, and down over the left flank and abdomen. A hematoma was present over the sternum at the site of the sternal biopsy, and a stab wound was present in the anterior axillary line, where a massive subpectoral hematoma had been drained surgically. The subpectoral area contained a large hematoma. The body cavities contained no blood. Our approach was limited to an abdominal incision. When the peritoneal cavity was opened, a large spleen presented, extending to about the brim of the pelvis in the midline. It weighed 3050 gm. The liver was moderately enlarged, weighing 2300 gm. Microscopically, the spleen showed very active myeloid metaplasia, with excellent maturation of all elements and many mature forms. The sinusoids of the liver also revealed hematopoiesis, chiefly of erythroid elements. The sections of bone marrow that were examined showed intense hyperplasia replacing all the fat; here, too, there was excellent maturation in all series. Large numbers of megakaryocytes were present in the marrow and spleen. The lungs demonstrated some atelectasis and emphysema, but there was no evidence of embolism or infarction. The left kidney weighed about 100 and the right 170 gm.; both kidneys showed fine granularity that was due to chronic pyelonephritis. In the pyramids of the kidneys there were white streaks, which proved on microscopical examination to be urates in the collecting tubules. This may be related to the fact, as Dr. Aub pointed out, that patients with polycythemia excrete considerable amounts of uric acid, probably owing to excessive nucleoprotein breakdown in the course of active erythropoiesis. As a matter of fact, cases of gout or gouty exacerbations have been described in association with polycythemia. There was an old thrombosis extending into the left iliac and left femoral vein as far as we could reach — the residue of the old phlebitis.

Dr. Aub: Why did she go into shock?

Dr. Freiman: As far as we could tell, it was due to the massive bleeding into the subpectoral area. The only internal evidence of bleeding was a small hemorrhage in the posterior mediastinum.

Dr. Aub: It does not take much there.

Dr. Freiman: Perhaps; but it did not seem to be producing any occlusion or compression.

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MEDICAL CARE AND INDIVIDUAL INITIATIVE

Elsewhere in this issue of the *Journal* Drs. McKittrick and Allen discuss the question whether the good of the American people demands compulsory health insurance. The opinions given and the conclusions drawn represent the physician's answer to those who advocate Government supervision and direction of medical practice. Interest in these papers is heightened by the fact that they were delivered before a lay audience.

Dr. McKittrick takes up in detail the arguments invariably advanced by the proponents of federal health insurance, presenting in rebuttal the facts as they appear to the majority of doctors. He reconsiders the comments on the state of the nation's health — so often interpreted and misinterpreted as to offer obfuscation rather than enlightenment — in terms of whether they prove that the Government's program is the only means of achieving the desideratum of the best possible medical care for the American patient. Thus, he finds no evidence that compulsory health insurance will improve the health of the nation, that it is necessary if medical services are to be furnished the "70,000,000 people . . . who . . . have difficulty in providing adequate minimal care for themselves and their families," or that it would meet the requirements of a good national program. He points out the danger that the proposed federal system "would eliminate any possibility of experimentation outside the structure of the compulsory, centrally controlled plan," and he offers the opinion that such a program would eventually lower the quality of care received. Finally, he states that the history of medical progress gives promise that the problem can be solved without sacrifice of the initiative and freedom that have raised American medicine to its present eminent standard.

Dr. Allen discusses the plan for better medical care in relation to what the profession has accomplished without the fetters and annoyances of federal dictation. He traces the progress in medical education, hospital standards and research that has made possible the present status of American health. He emphasizes the value of "the system of free enterprise" that has helped progress in medicine and other fields. In forthright terms, he recommends a program that will provide medical care for those who cannot afford to pay for voluntary health insurance: community co-operation among local taxpayers, the state and philanthropy, with federal taxation to meet the deficit.

The proposals advanced in these papers appear to have merits that compulsory health insurance lacks. The argument in favor of Government medicine concentrates on the needs of people who cannot afford to pay for voluntary health insurance but ignores the contribution of private philanthropy and voluntary community and state agencies to the care of the medically indigent. It makes much of doing away with a means test (accepted with apparent unconcern by those who benefited from the WPA and work relief but now somehow intolerable to the free American, or to those who pretend to speak for him) in a way that, absurdly enough,

would provide free care for the wealthy ne'er-do-well along with his less fortunate fellows; the burden, presumably, would fall on the man with a job, the inevitable scapegoat in ill considered programs.

The authors of the papers referred to are to be congratulated for their dispassionate but cogent presentation of the physician's side of the case. It should be evident to lay and medical readers alike that the physician's side is none other than that of the patient — the end in view is the good of the patient. It is high time the medical profession made its voice heard, not by its confreres but by the public, which in the final analysis will be the judge of what plan to accept or reject and what kind of medicine, Government or private, is best suited to its needs. The papers discussed offer assurance that the future health services of Americans can best be planned by those who provide the service.

DAMAGED GOODS

THE careful study by Ingalls and Prindle of 107 cases of esophageal atresia with tracheoesophageal fistula, reported elsewhere in this issue of the *Journal*, suggests many still unexplored possibilities in the etiology and prevention of congenital defects. Most spectacular among recent revelations of applied embryology has been the incontestable sequence of events between maternal rubella and certain well known anomalies occurring in the fetus. Equally challenging are such anatomic variations as those of the trachea and esophagus, nonfamilial and obviously not hereditary, yet occurring with a degree of regularity that has made such an investigation imperative.

Studies on human embryos have shown that these specific defects are present long before birth—as early, in fact, as the second month of fetal life. The broad pattern of tracheoesophageal fistula, which indicates a departure from normal sequences of development occurring at about the fifth or sixth week, is apparently similar to that of seventh-week or eighth-week origin previously described for mongolism. This similarity suggests that these particular defects in the embryo may be caused by any of a number of possible mishaps, in themselves unrelated but exerting the same kind of effect on the differentiating tissues. The anatomic structures involved are those that take shape at approximately the above-mentioned embryonic age.

The agents to be tested as causes of the anomalies are grouped in three categories. These are infectious agents such as rubella and syphilis, chemical agents such as nutritional deficiencies and toxic and metabolic disturbances, and such physical agents as mechanical trauma and structural disease of the uterus. In no case did the tracheoesophageal defect appear in successive generations or recur in the same generation of a family. Suggesting the diversity of the defects resulting from rubella were the associations also observed with anomalies of the cardiovascular, gastrointestinal, genitourinary, respiratory and skeletal systems.

The observation that illegitimacy was associated in an unusually large percentage of the cases studied suggests the possibility of an occasional connection with attempted abortion by mechanical or chemical agents. Instead of the abortion being accomplished, the fetus was possibly rendered defective.

The hypothesis that has been developed is that certain commonly grouped defects representing deviations from normal development during the second month of embryonic life are caused by agents acting through the mother and placenta. This hypothesis must be further tested, for "the question at issue not only is one of specific etiology but also involves principles underlying the larger phenomenon of acquired congenital malformations." Such testing can only be done effectively by a team, the members of which possess collectively more skills and training than any one man can usually master in a lifetime. The authors have availed themselves of the lifetime experience of Dr. Frederick T. Lewis in the field of embryology. The 18.1-mm. embryo featured was considered as "probably normal" for thirty-eight to forty days in C. S. Minot's *Textbook on Embryology*, published in 1910. Its sections, one of which is reproduced for the first time in this issue of the *Journal*, provided perhaps the first recorded case of tracheoesophageal fistula in a small embryo.

EMETINE IN ALCOHOLISM

THE publication, elsewhere in this issue of the *Journal*, of a fatal case following the use of emetine hydrochloride in the conditioned reflex treatment of chronic alcoholism sounds a timely warning. Emetine is a drug that may on occasion be toxic to the myocardium, presumably in proportion to the patient's sensitivity to it, and certainly in proportion to the dose administered.

Toxic manifestations of the severity reported by Dr. Kattwinkel are fortunately rare. Patients should, nevertheless, be subjected to the most rigid regime when on this treatment.

Dangerous reactions to the drug may be avoided, as suggested by the author and other authorities, by careful preliminary examination of the patient, including an electrocardiogram, in order to eliminate obviously poor risks; by his absolute rest in bed during the course of treatment and for the following four weeks; by careful observation for the signs or symptoms of diarrhea, fatigue, dyspnea on exertion, muscular tremors or weakness and dizziness; and by repetition of the electrocardiogram after the fifth grain of emetine has been administered, at the completion of the course of treatment, and two or three weeks later.

These precautions make the treatment reasonably safe as demonstrated by the large series of patients treated at the Washingtonian Hospital in Boston and at the Shadel Sanitarium in Seattle, Washington. Observations at the Washingtonian Hospital indicate that even in the rare cases in which cardiovascular and other manifestations have occurred, adequate measures, when instituted early enough, have led to complete recovery of the patient from the toxic reaction.

THE SHORTAGE OF NURSES

THE April and June, 1949, issues of the *Harvard Medical Alumni Bulletin* contain a remarkable essay entitled "The Shortage of Nurses." It is that part of the reminiscences of Harvard's oldest alumnus which is pertinent to this aspect of medical care. This is no new issue, but one with which the medical profession and the community have contended, with varying success and much failure, over a long period. Here an eminent physician whose experience spans an eighty-year period, and whose memory in his nineties is remarkably lucid, tells of his effort and that of others to establish what the doctors of this century have come to accept as a standard institution — the training school for nurses.

One may not conclude that Dr. Worcester altogether approved of developments as they took place. It is well known that the emphasis placed upon hospital schools for hospital purposes met with his vigorous warning, and he has long believed that with few exceptions the needs of the community were being neglected. Although it is true that the hospital has tended to neglect the needs of sickness in the home, it has on the other hand taken upon itself the responsibility of caring for many disorders formerly confined to home care.

In many communities this tendency has created a new paragraph in the minimum standard of living. Particularly in the urban areas, the people have come to consider that hospital care is an essential and inevitable service, to a much greater extent than it used to be and, perhaps, than it actually needs to be. The coming of the Blue Cross and the propaganda for "free medical service" is bringing to the minds of vast numbers of people a realization that hospitals are expensive places in which to live. The training of nurses in hospitals was once considered an economic stratagem, but it is no longer so. The training of nurses has become so expensive that many hospital schools are now silently folding their tents.

Dr. Worcester's reminiscences have a peculiar historical and practical significance at this time. They indicate a primary responsibility on the part of the medical profession that his generation recognized and carried. Is nursing still fundamental to the care of the sick? It is true that times have changed, and there are different problems to contend with, but somewhere the same zeal, the same burning desire to find a better way, if not a solution, to the present shortage is needed. For fifty years the medical profession has moved in the direction of raising educational standards for the training of nurses, at the same time resisting most serious attempts to produce another, less highly trained,

attendant type of nurse. Should it not consider moving now in the other direction?

The *Journal* salutes Alfred Worcester, for his long life of usefulness to others, for the enthusiasm with which he has met the challenges of the profession and for the clarity with which he has retained his interest in its problems.

CORRESPONDENCE

STATEMENT FROM MR. BARUCH

To the Editor: The statement has frequently been made that Mr. Bernard M. Baruch is in favor of compulsory health insurance. In view of this, will you be kind enough to publish the accompanying letter.

Dr. Madge C. L. McGuinness
51 East 87th Street,
New York, N. Y.

My dear Dr. McGuinness:

What I don't understand in all this talk about medicine is that everybody wants to go to the Government, even our own friends, to get aid. Yet they expect that the Government is not going to call the tune as long as it pays the piper. I certainly do not want to see what is generally known as socialized medicine. As I said at the time of my address, I would oppose it with all my might. I said, as you may remember, that the doctors have to get a move on themselves to meet the needs of the situation, and I stand on my speech. I know that men like Dr. Rawls are doing all they can to meet the needs of the situation without destroying the benefit the world derives from the great service the medical profession has always rendered.

Yours very truly,
(Signed) BERNARD M. BARUCH

MADGE C. L. McGUINNESS, M.D.
Chairman, Speakers' Bureau
Sub-committee of the Committee on Public Relations
Medical Society of the County of New York

THE NATIONAL HEALTH PROGRAM

To the Editor: Some months ago I received a letter from Dr. Channing Frothingham criticizing my inaugural address and threatening to go to the medical and lay press if I did not make retractions. This letter I did not believe it worth while to answer.

Dr. Frothingham states that compulsory health insurance will take care of the medically indigent. Mr. F. Donald Kingsley, acting Federal Security Administrator, according to the *New York Times*, made the following statement: "Those unable to work or dependent on public assistance could have their insurance premiums paid by various public or private agencies. Later we hope to find the means of achieving a complete one hundred per cent coverage of the population." Dr. Frothingham and his cohorts should get together.

Perhaps Dr. Frothingham considers the statements of his co-workers more authentic than the findings of the Brookings Institution. I don't. Regarding compulsory health insurance or socialized medicine, or both, Dr. Ernest E. Irons, former president of the American College of Physicians and president-elect of the American Medical Association has said:

To assert that the proposed program, as implemented in the Wagner–Murray–Dingell Bill, is not socialized medicine is no compliment to American intelligence. We are confronted with an attempt to impose socialized medicine on a people who do not want it. It is a fight that is much more than the fight for the freedom of American medicine. It is a fight for the preservation of American democracy and the American way of life.

Dr. Frothingham criticizes me for not finishing a quotation I made from Mr. Baruch's speech. The amusing part is that the Committee for the Nation's Health (Dr. Frothingham, chairman) has unfinished quotes on its pamphlet with Mr. Baruch's picture. For example: "The public is demanding better and more medical service through some action — political or otherwise." (Addendum: "*We must look for what can be done and do it. The great question is how? I do not want to seem to say I know the answers.*") "It can be devised, adequately safeguarded, without involving what has been termed 'socialized medicine.'" (Addendum: "The means can be met as in other fields, without the government taking over medicine — *something I would fiercely oppose.*") Dr. Frothingham states that Mr. Baruch proposed compulsory health insurance. That is not true. He did not advocate a compulsory health insurance scheme as envisaged by Dr. Frothingham or the Wagner–Murray–Dingell Bill. Mr. Baruch stated: "*For those who cannot afford voluntary insurance*, some form of insurance partly financed by the government covering people in by-law, I would call this compulsory health insurance, if that term's proper meaning had not been lost. . . . What troubles me most are the needs of that sizable segment of society *which does not earn enough to pay for voluntary insurance.*"

Dr. Frothingham gives a list of what he terms prominent people who are in favor of compulsory health insurance. Two of these were listed as sponsors of the recent cultural peace conference held in New York. Three doctors listed as sponsors of the conference are also listed as directors of the Committee for the Nation's Health. The papers during the conference were sufficiently explanatory, and nothing I might add would be more informative than the statements of the State Department, the press and the placards of the pickets.

In view of the happenings of recent months, does anyone question that employees of the Social Security Board are agitating for compulsory health insurance? Are employees of the Government paid to agitate or lobby for anything that is not a law of this country?

Concerning the Tokyo Mission, Mr. Harness quoted a letter from Mr. Wandel, which said in part, "We now think that our need is for someone who is primarily not so much an economic analyst as one versed in health insurance. Health insurance is the major field of social security in Japan . . . permanent revision requires amalgamating National Health Insurance with Health Insurance *on a compulsory basis.*" Do we need more?

The Committee for the Nation's Health is a lobby and employs paid lobbyists. My purpose was to publicize this fact. I have accomplished my purpose.

I could refute all Dr. Frothingham's statements, but they are so utterly without foundation that to do so would be a waste of my time and of valuable space in your journal. Suffice it to say that my inaugural address has served to awaken the medical profession in New York. Dr. Frothingham and his cohorts are disturbed over my address because it gives facts that they cannot refute. We know and understand their tactics and are not afraid to meet them anywhere, any time, any place. We have them on the run, and all their unfounded claims are comparable to an animal in its death throes that lashes out in all directions. But let me warn those who would destroy the freedom of medicine and eventually all freedom in this country that we haven't yet begun to fight.

WILLIAM BRYANT RAWLS, M.D.

Medical Society of the County of New York
2 East 103rd Street
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NOTICES

ANNOUNCEMENTS

Dr. Franklin P. Lowry announces the removal of his office from 313 Washington Street, Newton, to 62 Walnut Park, Newton, on July 1.

Dr. James G. Simmons announces that Dr. Fred W. Benton is now associated with him in the general practice of medicine at 30 Myrtle Avenue, Fitchburg.

(*Notices concluded on page xv*)